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## LIST OF CONTRIBUTORS

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DONALD C. BALFOUR, M.B. (TOR.)  
E. H. BECKMAN, B.S., M.D.  
J. M. BLACKFORD, M.D.  
WILLIAM F. BRAASCH, B.S., M.D.  
ALBERT COMPTON BRODERS, M.D.  
R. D. CARMAN, M.D.  
GEORGE B. EUSTERMAN, M.D.  
CARL FISHER, M.D.  
H. Z. GIFFIN, B.S., M.D.  
CHRISTOPHER GRAHAM, M.D.  
FLORENCE HENDERSON (R.N.)  
M. S. HENDERSON, M.B. (TOR.)  
E. S. JUDD, M.D.  
WILLIAM HOWARD LEWIS, M.D.  
WILLIAM CARPENTER MACCARTY, B.S., M.S., M.D.  
JUSTUS MATTHEWS, M.D.  
CHARLES H. MAYO, A.M., M.D., LL.D.  
WILLIAM J. MAYO, A.M., M.D., F.R.C.S., D.Sc., LL.D.  
BERNARD FRANCIS MCGRATH, M.D.  
GORDON B. NEW, M.D.  
H. S. PLUMMER, M.D.  
A. H. SANFORD, M.D.  
W. E. SISTRUNK, M.D.  
ERNEST V. SMITH, M.D.  
FRANK SMITHIES, M.D.  
G. J. THOMAS, M.D.  
FRANZ WILDNER, M.D.  
LOUIS BLANCHARD WILSON, M.D.

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MRS. M. H. MELLISH, EDITOR



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## ALIMENTARY CANAL



## A PLEA FOR EARLY OPERATION FOR CANCER OF THE LOWER LIP \*

E. H. BECKMAN

In discussing the subject of cancer one must necessarily take into consideration our present knowledge concerning its etiology and growth, and the various attempts which have been made from time to time to cure the disease or to prevent its dissemination throughout the body.

In spite of the conscientious work of hundreds of trained pathologists and bacteriologists, and the multitude of reports which these men have given to the world with regard to the etiology of cancer, the cause of the disease is still unknown. However, as a result of the labor of these observers much data have been given concerning the growth and dissemination of cancer. These data have been of the utmost importance in governing the methods of treatment of cancer and in developing means for its control and cure. The fact that the cause of the disease is unknown has not stopped attempts to cure it or prevented great progress in this direction.

A study of the pathology of cancer indicates that there must be a period in its growth when it is limited to an extremely small group of cells in some part of the body, and while still so confined, can be cured by complete removal of this diseased area. We have also learned that cancer is disseminated throughout the body in almost every instance by metastasis along the lymphatic channels which drain the affected area, although there is evidence to show that dissemination may take place through the blood in certain

\* Read before the Oregon State Med. Soc., Medford, September 18-20; also before the Colorado Med. Soc., Glenwood Springs, October 7-8, 1913.

cases. Cancer may also be engrafted from one part of a cancerous subject to another by direct transplantation of the cancer-cells, but no instances are on record of a cancer having been transplanted from one subject to another.

In the abdomen, cancer-cells appear to become separated from the primary growth and transplanted to other parts of the peritoneal cavity. The early involvement in the pelvis in certain cases of cancer of the stomach can be explained in no other way. The diffuse involvement of the entire abdominal cavity following the rupture of a malignant ovarian cyst is another example of this process. These facts, while important and an aid in curing cancer, do not teach us anything concerning its origin.

Williams,<sup>1</sup> who has written extensively on this subject, believes that chronic irritation has no influence on the production of cancer. Other observers of equal standing believe that chronic or prolonged irritation is one of the important factors in the production of the disease. Cancers originating on the surface of the body never occur except at points subjected to continuous irritation over a considerable length of time. All physicians are familiar with the type which develops on a crack or ulcer of the lip, about a mole, a sebaceous cyst, in an ulcer, or the scars resulting from burns. There is evidence also to show that cancers inside the body always develop in tissues subjected to prolonged irritation. The stomach, with its acid content and the continuous irritation it receives from large, coarse particles of food, as well as the fact that it is nearly always overworked, is one of the most frequent situations for cancer. The large intestine, which also contains coarse dried particles of feces, and, in addition, has a high bacterial content, is frequently the site of the primary lesion. The small intestine, which is always practically empty, and when filled contains only liquids of a slightly alkaline or neutral reaction and a comparatively low bacterial content, is in direct contrast with the stomach and large intestine relative to the frequency of primary cancer. The one fact which seems to stand out above all others is that factors, such as tumors, ulcers, etc., which produce or aid irritation are often the primary site of cancer.

Cancer seems to be on the increase; if not on the increase, it certainly is true that more cases are being diagnosed than formerly, and larger numbers are being reported to the various health authorities. Because we are in ignorance of the etiology and have no means of preventing the disease certainly does not prevent us from curing it in the early stages. Our only hope lies in the dissemination of knowledge which we have regarding its development, and in this way teaching the public to come earlier for observation in any suspected case.

Our present knowledge concerning the cure of cancer is relatively as follows: The most enthusiastic internists are willing to admit that there is no medical cure. Paste containing arsenic is one of the oldest methods of treatment. These pastes have no selective action for cancer, but do have some affinity for pathologic tissues, probably because such tissues contain more water and have less vitality than normal tissues. We know that paste can simply eat out a localized area where it is applied, but cannot possibly have any effect after the growth has left the primary focus.

The Roentgen-ray, after years of application in cancer, has not given the results which were hoped for it. It has no direct effect except that it stimulates the formation of fibrous tissue and in this way delays the growth. Radium is still in the experimental stage as regards treatment. Its effect is probably similar to that of the Roentgen-ray. It has no effect on a growth situated on the mucous membrane.

If applied with intelligence in the early stages of cancer, surgery nearly always produces a cure. Late surgery simply delays. In considering surgery as a treatment, the essence of cure is time, if other factors are equal. The public should be educated in regard to these facts, and it should be impressed upon the people at every opportunity that the disease and not the treatment is dangerous. The danger comes not from operation, but from delayed operation.

In order that cancer may be cured by surgical measures the lesion must be so situated that an early diagnosis is possible. It must also be so situated that the growth itself can be removed

with a wide margin, and the lymphatics into which this area drains should be accessible for removal at the primary operation. Cancers of the lower lip are ideally situated to conform to these points. In addition, they are usually slow-growing, with but slight tendency to form metastasis in distant parts of the body. The chain of lymphatics about the neck is so abundant and guards this area so well that it is only on rare occasions that a metastasis is allowed to occur beyond them. In these cases the patient is aware of a lump, an ulcer, or a crack which does not heal, and medical advice is sought. While a correct diagnosis can be made in most instances by observation, the only absolute proof is a microscopic examination by a competent pathologist. Too many cancers of the lower lip are regarded as specific ulcers by the physician, and valuable time is sacrificed in trying out the effect of potassium iodid. It should be remembered that a syphilitic ulcer of the lower lip is an extremely rare condition, and that cancer is exceedingly common. Any physician in America, no matter how isolated he may be, can send a specimen to a pathologist and get a telegraphic report within a few days. Only when we come to realize the importance of an early diagnosis will we appreciate the necessity of a correct pathologic diagnosis. The important factor in these cases is time, and in almost every instance the patient can be cured if the diagnosis is made early. The only cases which are hopeless are those patients who have delayed so long that an operation is no longer advisable.

The area of drainage of the lower lip is so well established and has been so carefully studied by competent observers (Poirier, Cuneo, Küttner) that one knows definitely the lymph-nodes which are first affected after the cancer has progressed beyond a local disease. The submental glands, lying in a triangle bounded by the anterior bellies of the digastric muscles and the hyoid bone, drain the central portion of the lower lip. The submaxillary glands, which lie in the submaxillary triangle, bounded by the digastric muscle and the ramus of the lower jaw, drain the remainder of the lower lip, as well as the anterior portion of the cheek. These triangles drain the entire lower lip, and if the glands are



removed early, a complete block between the primary focus of the disease and the remainder of the body is effectually established. It sometimes happens that the submaxillary lymphatics on the side opposite the cancer become involved. While this occurs but rarely, one should remember that when the regular lymphatic channels are blocked, whether by cancer or inflammation, the lymphatic stream may flow in any direction, similar to the blood being taken up by the collateral circulation when the main trunk of a vessel is ligated. Thus it is necessary in every case to remove the lymphatics on each side at the primary operation. This should include the submaxillary salivary glands also, not because they become involved by the cancer, but because it is impossible thoroughly to remove the lymph-nodes and leave the submaxillary salivary glands.

After the glands from one side have been removed, they should be examined microscopically at once, and if involved with cancer, the dissection should be carried down that side of the neck. This is the so-called "block dissection," and is best done by including the sternomastoid muscle, which allows better exposure and enables one to do a more thorough dissection. The dissection should include all the glands and gland-bearing fascia of the entire neck, including the anterior and posterior deep jugular glands. Butlin pointed out the importance of the area underneath the sternomastoid muscle and posterior to the submaxillary triangle, actually the posterior part of the submaxillary triangle lying near the mastoid portion of the temporal bone. This is a point at which glandular recurrence following operations for cancer of the lower lip frequently takes place, and which may be overlooked in making the dissection.

The principle underlying the cure of cancer of the lower lip is the same as that involving the cure of cancer in any other part of the body; that is, the primary growth along with the glands into which the area of the growth drains must be thoroughly removed at the earliest stage possible. The medical profession too long has assumed that cancer of the lower lip is not as malignant as cancers in other parts of the body, and has contented itself with

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conservative measures when radical surgery was imperative. A physician who is not competent to do a thorough dissection of the neck is not fitted to treat a cancer of the lower lip.

There is one differentiation to be made between cancer of the lower lip and cancer in other parts of the body. A cancer of the lower lip is either a local growth or a metastasis in the adjacent glands. I have never observed a cancer occurring in the lymphatic vessels between the original growth and the lymphatics of the neck; consequently, it does not seem necessary to remove these vessels along with the glands and the primary growth. This is fortunate for both the patient and the surgeon, because it lessens the danger of infection from the mouth into the deep tissues of the neck. The original growth, however, should be removed with a wide margin—the wider the better.

In cases where only the submaxillary and submental regions have been dissected, infection is not of serious consequence, since the mouth may often be entered in these dissections, and also because infection occasionally takes place from the mouth through the cut duct of the submaxillary salivary (Wharton's) gland. In cases where the dissection must extend along the jugular vein to the clavicle, we prefer to perform the operation in two stages, in order to lessen the danger of infecting the entire deep tissue of the neck. The extensive skin-flaps which are necessary in the block dissection heal very satisfactorily, but if infected from the mouth, the fascia has a tendency to slough and convalescence is delayed materially.

Our customary procedure in operating for cancer of the lower lip is illustrated by Figs. 1, 2, and 3. An incision is made  $\frac{3}{4}$  inch below the ramus of the jaw, from one sternomastoid muscle to the other. This incision extends through the skin and platysma muscle, and is made low in order to avoid the small branch of the facial nerves, which swings down below the angle of the jaw and then returns on the face to supply the muscles about the angle of the mouth. When it is necessary to remove only a small portion of the middle of the lip, a better cosmetic result is obtained by saving these branches of the facial nerves. If, however, it is neces-

sary to remove more of the lower lip and widen the mouth by extending into the cheek, it is not necessary to save these nerves. Through this incision the skin and platysma muscle are reflected down to the hyoid bone and up to the inferior maxilla.

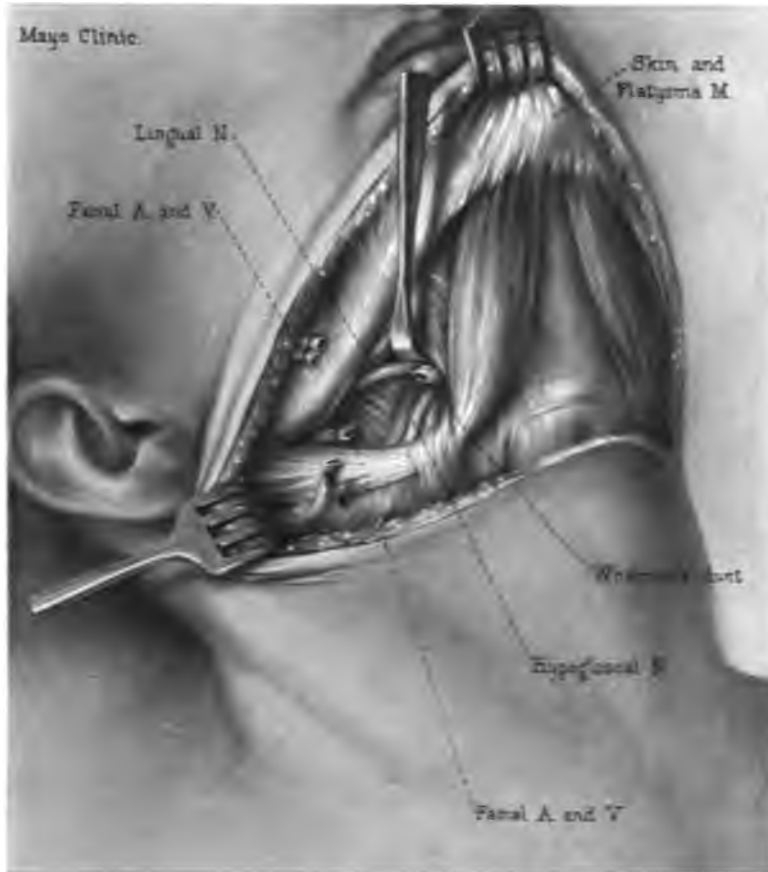


Fig. 1.—Dissection of submental and submaxillary triangles for epithelioma of the lower lip.

All the fascia and fat, including the submaxillary salivary glands, are removed from the submental and submaxillary triangles (Fig. 1). It is necessary to ligate both the facial artery and

vein, and the blood-supply to the face is so abundant through the other branches of the external carotid that sloughing will not occur from this cause. The hypoglossal nerve and the lingual branch

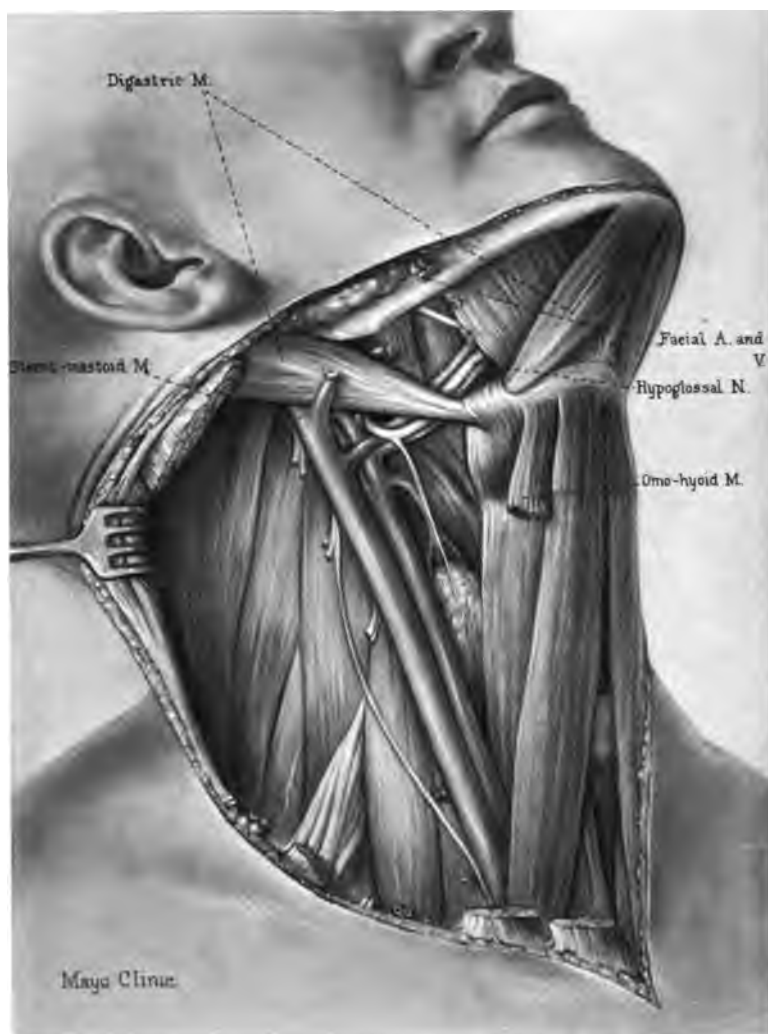


Fig. 2.—Block dissection, with removal of sternomastoid muscle, employed when submaxillary glands are carcinomatous.

of the trifacial are exposed on each side and should be saved. After the removal of the glands this primary incision is closed, drainage being established through small separate incisions on either side. The platysma muscle is stitched first, and then the skin with a

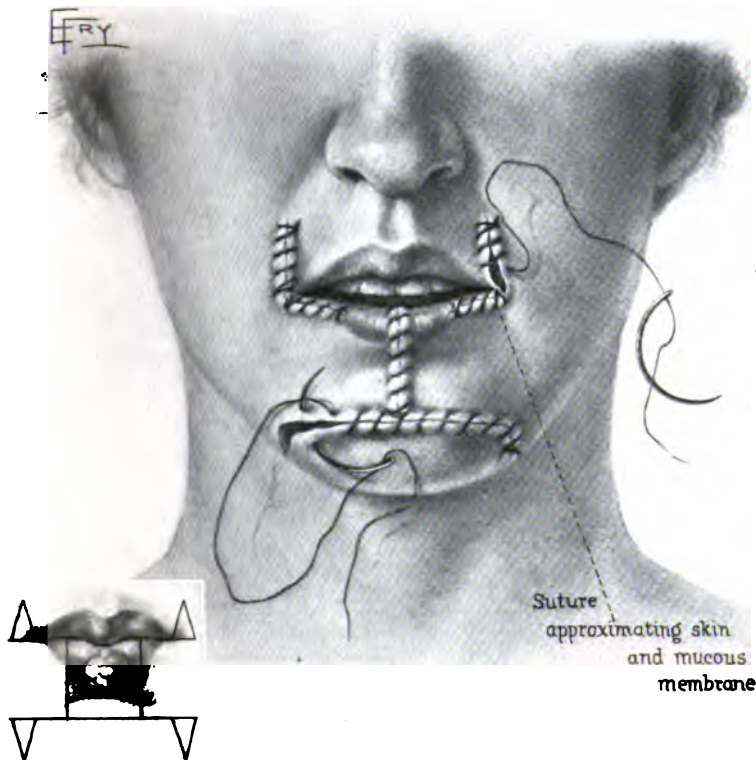


Fig. 3.—Illustrating plastic operation for removal of a portion or the entire lower lip for cancer.

subcutaneous suture. The wound in the neck is carefully protected, and the operation on the lip begun (Fig. 2).

A quadrilateral section, including the full thickness of the entire lip, is removed, running down nearly to the point of the chin. The section removed should include the growth and from  $\frac{1}{4}$  to  $\frac{1}{2}$  inch on either side into the healthy tissues. The coronary artery

should be tied on either side. An incision is then made from the lower angle of the quadrilateral parallel to the ramus of the jaw on either side as far as is necessary to obtain enough tissue to close the defect. The entire flap from which the new lower lip is to be made should be freed well from the bone. These flaps are sutured together in the midline with silkworm-gut sutures, the skin being approximated with horsehair. If the skin remaining over the point of the chin is so long when approximated to the new lip that



Fig. 4.—Patient one week after having had one-half of the lower lip removed for cancer.

it produces wrinkles, it is shortened by taking out a small triangle at one or both ends of the incision. This is the technic employed in cases where only a small portion of the lip is removed (Fig. 3). If it is necessary to remove one-half or more of the lower lip, the primary incision is made in precisely the same manner. In addition to the incision running from the lower end of the quadrilateral piece along the ramus of the jaw, it is necessary to make incisions parallel to the former, extending from the corners of the mouth

directly into the cheek. These incisions should extend slightly downward, rather than upward. The suggestion of J. Clark Stewart to incise through all the tissues except the mucous membrane, then incise  $\frac{1}{4}$  inch higher and cut through the mucous membrane, is a valuable point in the technic, since it gives plenty of mucous membrane to stitch over the raw surface of the lower lip and thus prevents contraction of the mouth. When the flaps on each side are thoroughly free, they are approximated as in the



Fig. 5.—Patient one week after having the entire lower lip removed and plastic operation as per Fig. 3.

former case, the only difference being that the raw surface of the lower lip must be covered with mucous membrane, as just mentioned. It is now seen that the lower lip is shorter than the upper, and also shorter than the skin remaining on the chin. These two latter are shortened by removing triangular pieces from the extremity of each incision. This plastic work was taught me by C. H. Mayo, and I have not seen it described in the literature (Figs. 4, 5, and 6).

From January 1, 1907, to January 1, 1912, there were 199 patients with cancer of the lower lip observed in the Mayo Clinic. This number includes only those patients having a cancer confined to the lower lip, or one which had apparently originated in that location.

Twenty-five cases were diagnosed from clinical observation alone; consequently they cannot be proved to have been cancer.



Fig. 6.—Patient three weeks after removal of the entire lower lip and plastic operation as per Fig. 3.

Two of these patients had had the local growth removed from the lip before coming to our clinic. From the histories it appeared certain that the condition had been cancer, and it was thought best to remove the glands. This was done, and both patients are well without signs of recurrence. Seventeen patients in this series were considered inoperable when first seen. Two others refused operation, and four are not accounted for. This makes up the group of 25 cases in which we have a clinical diagnosis alone. The remaining 174 cases of proved cancer which form the basis of my report have both clinical and pathologic findings.

One hundred and twenty-six patients had a radical operation performed as the first operation. Ninety-nine of these have been traced; letters have been received from some; others have been examined within the past few weeks. Twenty-seven of the group have not been heard from. Of the 99 patients heard from, 83 have no sign of a recurrence either locally or in the glands of the neck. Sixteen have either died of their original trouble or now have a recurrence. Seven of these 16 patients had glands involved



at the time of their operation, and 3 others had an extensive growth on the lip.

Considering only the patients concerning whom we have obtained definite information, that is, the 99 patients from whom we have received letters or who have been examined, 83 of whom are cured, we have a percentage of cures following a primary radical operation for cancer of the lower lip of 83.8 per cent. It is interesting to note the time since the operation on these 83 patients. Two were operated on one year ago; 25, between one and two years; 17, between two and three years; 20, between three and four years; 15, between four and five years; and 4, over five years. In 18 of the above number glandular involvement was demonstrated by the microscope at the time of operation, and 9 of these, or 50 per cent., are among the cured.

In another group have been placed 25 patients who had a late radical operation, that is, removal of the glands of the neck following one or two local operations on the lip or following treatment by paste.

Twenty of these patients have been traced. Fourteen are classified as cured and 6 as not cured, giving a percentage of 70 per cent. of cures of those patients having had a late radical operation, as compared with 83.8 per cent. cures of patients having had primary radical operations.

In 12 of the above 25 patients glandular involvement was demonstrated by the microscope at the time of the operation; 4 of these are cured. While this group of 25 is much smaller than the previous group, it is interesting to note that when the radical operation was delayed, only a third of the patients having glandular involvement were cured, as compared to 50 per cent. of cures in those having glandular involvement following a primary radical operation.

In five of the patients removal of the glands either as a primary or secondary operation was incomplete. These patients have been traced. In this group are cases in which an operation was attempted but abandoned because the involvement was found to be so extensive. It also includes cases in which glands were removed from

but one side of the neck, the growth in the lip being confined entirely to one side. Two of these patients are well, with no signs of recurrence.

In a last group consisting of 18 cases we have placed those patients having had an excision of the local growth without the removal of glands. Most of these patients were seen early in the disease, but their general condition or age prevented a radical operation. Fifteen of these have been traced and 11 are cured, giving a percentage of 73.3 cures.

It has been stated by other observers or borne out by statistics that an early operation for cancer, although not a radical one, is often more favorable than a late radical operation. This holds true in the present series, as 73.3 per cent. of the patients having an early local excision were cured, as compared with 70 per cent. of cures among those who had a radical operation in the late stage of the disease. There were no operative deaths in this series of cases.

#### CARCINOMA OF THE LOWER LIP

GROUP	NUM- BER OF CASES	NUMBER OPERATED	TRACED	NOT TRACED	CURED	NOT CURED	INOP- ER- ABLE	PER CENT. CURED
I. Clinical diagnosis only ..	25	2	6	19	2	23	17	..
II. Primary radical opera- tion .....	126	126	99	27	83	16	..	83.8
Glands involved .....	18	18	18		9	9	..	50.0
III. Late radical operation ..	25	25	20	5	14	6	..	70.0
Glands involved .....	12	12	12	0	4	8	..	33 $\frac{1}{3}$
IV. Glands removed one side or incomplete .....	5	5	5	0	2	3	..	40.0
V. Local excision only .....	18	18	15	3	11	6	..	73.3

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## CONSTITUTIONAL DISEASES SECONDARY TO LOCAL INFECTIONS \*

CHARLES H. MAYO

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The present period will live in history as the age of science. Life is the law of the universe and represents the mysterious forces which perpetuate the species, the study of which forces leads one to an adequate conception of the meaning of life as applied to the existence of the human race.

The lowest forms of life, or unicellular organisms, increase by division only and thus live on indefinitely. Each division or half cell becomes complete and continues to carry on the process. By breaking up into granules these cells may appear to die, but the granules are frequently spores which live on until, in their proper environment, they again develop cell-form and the process of division goes on as before. Such life is not terminated naturally, though it may be destroyed.

Death entered the world as the termination of a higher type of life of the multicellular organisms. In this form the continuance of the process is carried on by certain germ cells which have a definite function and are set aside for this purpose. The life of this higher organism comes to an end naturally through an exhaustion of the processes of nutrition, excretion, etc. The circulatory, respiratory, and, to a lesser degree, the nervous systems, the automatic control of which lies in the glands of internal secretion, are each necessary for the maintenance of such an organism, but each in turn may be destroyed, thus bringing about dissolution of the whole.

The multicellular organism is both a unit and a compound of

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many tissues, any of the special groups of which may be deranged in function or destroyed with varying effect on the whole, according to their respective values. The somatic death of the whole organism through cessation of the vital functions is not necessarily followed by the immediate death of the various cells composing them. For example, the cells may live on in skin, nerves, etc., which have been transplanted from a dead member or a dead body, as is demonstrated in surgery of the present day.

The body may be looked upon as an intricate machine, the glands of which exist for the purpose of nutrition, defense or elimination, their function being manifest through the action of their hormones or chemical messengers which are delivered into the blood for action, the natural association of all being completed by their connection with the sympathetic nervous system.

At birth the child's intestinal tract is free from bacteria, but within a few days the digestive system is invaded by them and remains so throughout life. In an examination of the intestinal secretions of 1000 individuals with gastro-intestinal symptoms by Sanford during the year 1912, about 10 per cent. showed protozoa in addition to the usual intestinal bacteria. Only about half of these, however, are known to be causative factors in the production of disease.

From the time of birth, then, and even before animal life continues alone, its destruction is prevented only through maintaining a vigorous conflict against bacteria and protozoa. Man is subject to the constant attacks of diplococci, streptococci, staphylococci, the various groups of bacilli and many varieties of protozoa and insect parasites. Such battles royal against an invading army present fields of destruction quite as devastating to the tissues and elements in the blood of the host as are those of the wars of nations. This destructive invasion changes the arteries, the function of the heart, kidneys, etc., and finally, after making life uncomfortable, brings on a premature old age, due to an exhaustion of nutritive supplies, to a weakening and devitalizing of defenses, until the army of phagocytes retire defeated by death, the conqueror of all things.

It is difficult to understand why such destroying agents or even the annoying ones should have a place in the economy of the universe. However, were it not for such agents life might be continued so long as to be valueless and necessitate termination by the public executioner.

So much is said concerning the activities of deleterious bacteria that we almost forget the fact that they are but few in number as compared with the enormous group engaged in useful occupations. Through fermentation some of these bacteria develop agents useful for art as well as science. Others split up inert and dead tissues into their original elements, that they may again become useful. Much of our plant life and agricultural processes could not go on without the nitrogen-forming varieties of bacteria. We are unfamiliar with many of these life-giving processes; some are said to be harmless and we may later find them useful as well. Moreover, the further we investigate these agents which appear bent on the destruction of our peace and happiness, the more do we come to believe that the diseases they inflict are preventable and under the control of individuals through attention to cleanliness, hygienic laws, etc. Were it not for the presence of bacteria, care of our food and our bodies would be unnecessary. Thus, they have their place in the evolution and advancement of civilization.

With our present absolute knowledge of the specific organisms of so many diseases, is it too much to suppose that all diseases may have a specific cause? Possibly this may be true with the exception of congenital defects, injuries, chemical irritants, and neoplasms. The latter may still be brought into this class as caused by infective agents.

The study of these minute forms of vegetable and animal life is most fascinating and one which is pursued by scientists the world over. The mass of knowledge which has been accumulated is bewildering and, since fame is so closely associated with the discovery of new species, it requires the constant attention of the student to determine whether these announced discoveries are of a new species or but a mere variation in type.

Great progress was made in our knowledge and understand-

ing of disease when Virchow published his work on the study of cellular pathology, which marked a distinct epoch in the history of medicine and focused our attention on the cell instead of the organ.

Diseases due to derangement in the function of various organs of the body have been termed autointoxications, *e. g.*, thyroid intoxication. In considering the diseases due to infection other than the well-known infective fevers, the word autointoxication has been quite generally, though wrongly, used to interpret symptoms supposed to be due to the absorption of toxins produced by local septic processes. While such toxic absorption plays a part in the production of disease, it is true that in most diseases due to infection the living bacteria pass into the blood and through their activities and death cause irritation and fermentation in the blood itself. Some of the bacilli act as parasites on the blood-cells. They may be carried in clumps, causing septic infarcts in the periphery of the lung, especially when the gastro-intestinal mucosa is involved. From the septic tonsil such deposits may be made in the bones, causing osteomyelitis.

It is only recently that we have begun to appreciate how common is the direct contamination of the blood by living organisms. Formerly only the more serious conditions of pyemia and septicemia were recognized as caused by living bacteria in the blood. Such general infections are now known to be a source of disease and the blood may contain many living bacteria, such as pneumococci, streptococci and staphylococci, and various bacilli. Bacteria in the blood may produce either very great or very little effect as externally manifested.

The portals of entry of pyogenic micro-organism into the body are numerous. While it is possible to gain entrance through wounds and abrasions of the skin and mucous membranes, it is apparently possible for some varieties to affect uninjured surfaces as well. Garré applied a small poultice of the staphylococci to the healthy skin of his arm and produced a carbuncle.

Bacteria may enter the common bile-duct from the intestine; more frequently they pass the intestinal wall and appear in the portal circulation. The urethra has its special bacterial flora and

the genital tract may also be invaded by the intestinal bacteria. The nasal cavity has its special group, though, unless the mucous membrane be diseased, this cavity acts as a vacuum cleaner on the air-borne germs. The major portion of pyogenic micro-organisms affecting the body must then enter the mouth (Figs. 7, 8, 9, 10). The tonsils with numerous open crypts drain into large lymph-channels, and while they are defended by numerous police in the form of wandering leukocytes, these defenders, because of other

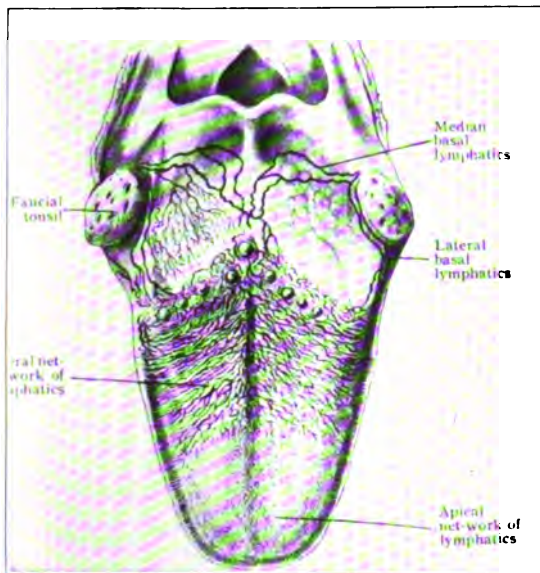


Fig. 7.—Lymphatics of dorsum and margins of tongue (from Küttner).

demands or general temporary depression, may be off duty at a critical moment.

In the mouth we find that the teeth are subject to infective destruction frequently under pressure. Root abscesses are developed from diseased pulps of teeth. These frequently give no symptoms, and often are not suspected until their presence is revealed by the x-ray during an attempt to locate some obscure local infection (Fig. 11).

That scourge of the human race, pyorrhea, accounts for an enormous amount of infection of the blood. In a recent paper Hartzell describes pyorrhea as inflammation of the margin of the gum, with destruction of the underlying bone. He discusses at length the work of Talbot and the early history of the disease before the period in which Dr. Riggs' name was associated with it through his efforts to overcome the infection. The recent advances in the study of pyorrhea show that 80 per cent. of these cases can



Fig. 8.—Lymphatics of tongue (from Poirier)

be healed by treatment and that most of the others can be held in check by continued treatment. In some cases removal of the teeth is necessary to accomplish a cure. Removing the teeth prevents harboring certain bacteria, thus removing a focus of infection.

Smithies has recently made a routine examination of the mouth, teeth, tonsils, and saliva of 318 patients who presented themselves



in our clinic for test-meal examination because of gastric disturbances. Similar examinations were made, as controls, of the mouths of 16 other persons selected from laboratory assistants, nurses, and physicians.

Of the 334 individuals examined, but one-fourth of the number were found to have good teeth, while more than one-half of them had inferior or diseased teeth. Two hundred and one (60 per cent.) showed erosions of the teeth, gum-margins, or a definite pyorrhœa alveolaris (Fig. 12). Twenty-seven per cent. of the cases in which the tonsils and nasopharynx were examined showed enlargements,

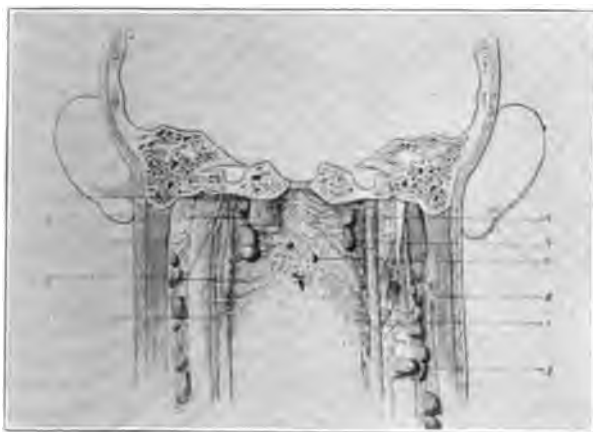


Fig. 9.—Retropharyngeal glands (from Piersol's Anatomy).

crypts, exudate, or erosion of the tonsils, 19 per cent. gave evidence of nasopharyngeal inflammation, and in 3 per cent. there were ulcerative conditions of the oral mucosa apart from adenoid hypertrophy or pyorrhea.

The chemical examination of the saliva showed the presence of an enzyme similar to that found in the stomach which causes the cleavage of the dipeptid glycytryptophan in a large majority of the specimens. It was noted, however, that the amount of this enzyme seemed to be greatest in those patients having the most infected mouths. It was also shown that cultures of bacteria

grown from salivas, when added to salivas in which the enzyme had been destroyed by heating to 100° C. rendered such salivas again capable of splitting the dipeptid. These experiments seemed

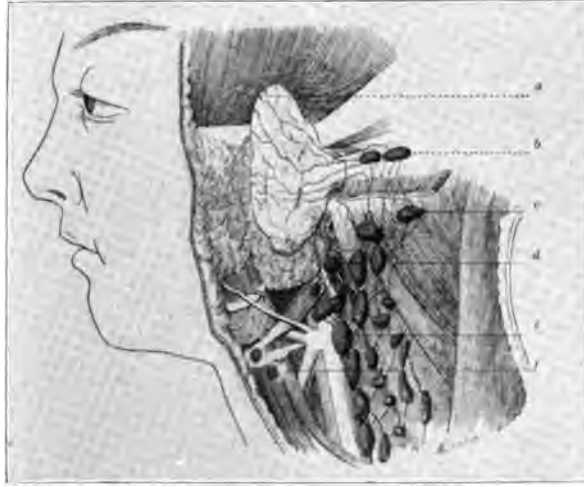


Fig. 10.—Deep cervical chain (from Piersol's Anatomy).



Fig. 11.—Mandible with the cortical portion of bone removed from the body.

to furnish evidence first that a large proportion of patients with gastric trouble have infected oral cavities, and, second, that this infection is in direct relation to the formation of a peptid-splitting enzyme in the saliva.

Those individuals suffering from diabetes and rickets and women having repeated pregnancies are especially prone to pyorrhea. It will also be found prevalent in individuals during epidemics and in pet animals or those in confinement.

We must, therefore, look upon the disease from a wide point of view. A number of bacteria are found normally in the mouth; neglect and disease may greatly increase them. Matzuschita found 60 different varieties of these bacteria and Miller found 29



Fig. 12.—Advanced pyorrhea alveolaris (from Hartzell).

varieties. Professor Black, who is so often credited with giving the first as well as the last word in dentistry, believes that the common varieties which are to be considered in diseased conditions, some of which are constant, but many varying in number, amount to about one-fourth the highest figure. He also believes that the deposits of tartar, which favor the development of bacteria, are often caused by overfeeding and overnutrition. Foul odors are caused by the indol-forming group, sweet odors by the yeasts.

Hale White, Osler, Billings, and many other noted internists have written on the subject of systemic diseases arising from infections of the mouth. Looked at from every standpoint, the mouth may be said to be the greatest portal of entry for pyogenic organisms. Many species and varieties find a foothold in the tonsils, lymphoid tissue of the pharynx, and about diseased teeth and gums.

There are three modes of bacterial distribution—first, by continuity of tissue, as in the eye, ear, and sinuses; second, by ingestion, by way of the stomach; third, by direct entrance of tissues and lymph-channels.

Microscopic examination of gastric extracts made by Smithies from 2406 different individuals with "stomach complaint" (dyspepsia, indigestion, and the like) showed that, irrespective of the degree of acidity of such gastric extracts, bacteria were present in 87 per cent. Morphologically, cocci and diplococci were present in 83 per cent.—short and long rods (often of the colon group) in 58 per cent.—typical streptococci and staphylococci in 17 per cent., and *Leptothrix buccalis* in 24 per cent. In 54 cultural studies of saliva from "dyspeptic" patients, streptococci and staphylococci were demonstrated in over 80 per cent., bacilli in 66 per cent., and *Leptothrix buccalis* in more than 14 per cent. Comparing these figures, it would appear that the common forms of pus-producing organisms (streptococci and staphylococci) have their proliferation retarded in gastric juice, but that bacilli (often of the colon group), as well as *Leptothrix buccalis*, thrive in the stomach.

Kelynack has called attention to the association of tonsillitis with appendicitis. Poynton and Paine report a case of appendicitis, which upon removal gave a pure culture of the same strain as that cultivated from a diseased tonsil removed at the same time. These streptodiplococci were injected into rabbits, causing arthritis, and the fluid removed from the arthritis again gave a pure culture. It is often noted that serious diseases of the tonsil cause few or no local symptoms.

Endocarditis is an infectious disease, producing vegetations and ulcerations on the valves of the heart and injury of some of the

larger vessels. This infection is carried to the circulation most frequently from the infected tonsil. Rosenow has shown that the bacteria are of a low grade of virulence, but tenacious of life. After repeated passage from animal to animal these cocci resemble pneumococci. By using strains cultured from the blood of such cases, and also from the tonsils in the same group, inoculating into the veins of rabbits' ears he could within forty-eight hours show lesions of the valves of the heart in more than one-half the cases, while others showed lesions from infected emboli in the lungs, kidneys, etc.

Wadsworth found that, in order to produce pneumonia in rabbits with pneumococci, it was necessary to have a properly balanced relation between their virulence and the resistance of the host. This is true of the human variety also, as the pneumococcus may be found in the mouths of about one-third of us.

Rosenow found positive blood cultures of pneumococcus in 132 out of 145 cases of pneumonia. Blood-smears were successful in 47 of these cases, in 3 of which the blood cultures had failed.

The valves of the heart become sclerotic from contraction caused by the many hemorrhages of embolic bacterial origin. Endocarditis is more common in the young than in adults, their susceptibility being increased by the presence of capillary vessels in the valves. Attacks in older individuals and later attacks in children lead to ulcerative malignant endocarditis, induced in the finer capillaries of the damaged valves, the relatively avascular condition of which protects the bacteria from the destroying effects of the leukocytes. The lymphoid tissues of children, in whom attacks of endocarditis and rheumatism are more frequent, possibly assume more importance than infected gums, which become more important as age increases. In a recent paper Hale White reports finding in the urine of patients *Bacillus coli communis*, streptococci, staphylococci, gonococci, pneumococci, bacilli of typhoid, etc. The bacillus most commonly found is *coli communis*, especially in the urine of pregnant women. Children, as we know, are frequently found to have the common intestinal bacteria in the urine, with but few symptoms. These are, moreover, almost accidental

findings, since in but few of these cases is the urine examined. High temperature in children without known cause is an indication for the microscopic examination of the urine. In some instances one kidney in a child may be destroyed by the colon bacillus. We discovered and removed one such kidney in a child five years of age. When such cases are observed late in life, it might appear that the individual was born with but a single kidney. The infection may occur through the genital tract or through the bloodstream, and rarely by direct penetration of the kidney. Since more than seven female children are affected to one male, this probably indicates that infection often takes place by way of the urethra. In one case the staphylococci found in pyorrhea were also found in the urine. In another case staphylococci were found in a boil, in blood, and in the urine. Pneumococcus has been found in the pyorrhea and in the urine. The *Staphylococcus aureus* was found in the gums and in the urine; the findings of such bacteria are often unaccompanied by pus, blood, or albumin.

According to Loeb and Bingham, acute nephritis is not uncommon following the infectious fevers of childhood other than scarlet fever, in which the frequency is well known. Lewis records the recent epidemic of diphtheria in the city and county hospital of San Francisco, showing that 12 nurses with tonsils developed the disease, and about an equal number of nurses whose tonsils had been removed did not develop it.

Murphy states that every type of non-traumatic inflammation of the joint is the metastatic manifestation of a primary infection in some other part of the body. In 1887 Mantel said he believed that rheumatism came from diseased tonsils. Since then many observers have proved the truth of his hypothesis. Frank Billings recently reported some cases of multiple arthritis in which the fluid withdrawn from the joint gave the same strain of streptococcus grown from pus removed from the tonsil. Removal of the tonsils cured the rheumatism. Coombs, in a study of experimental rheumatism, found the disease to be the same in rabbits as in man, and more readily developed in comparatively young animals. It was produced by cultures from vegetations from the valves of the

heart of a child dead of rheumatism. Rheumatic infections following local infections of gonococcus are well known. It is worthy of note that the local infection is held in temporary abeyance by the more serious infection of the blood. Long ago rheumatism was believed to be caused by the flow of fluids, and originally was described as the flow of spoiled fluids from the brain to other parts of the body. Catarrh was believed to be caused by the elimination of the fluid through the mucous membrane. These questionably wise sayings, handed down through many generations, still have their influence. Many laymen seriously fear the treatment of catarrh, believing that rheumatism may develop if the catarrh is cured.

Schichold reports 70 cases of rheumatism in which pus was found in the tonsils.

Libmann and Celler report the finding of pneumococcus, streptococcus, and *Streptococcus mucosæ* in the middle-ear infections. Kobrak found bacteremia to be a very significant diagnostic evidence of sinus thrombosis in middle-ear and mastoid diseases. They may be present in the blood in varying degrees for days or two or three weeks before other positive indications call for operation. They disappear from the blood within two days after operation and ligation of the jugular vein. They remain in the blood only if some other focus is established as an ulcerative endocarditis.

What, if any, are the factors of defense of the animal or the human being against pyogenic micro-organisms which have gained entrance to the tissues of the body? Wright states that no one acquires protection against disease save by the production of protective substances; that no one can live in the presence of infection save by the aid of these protective elements, and that no one recovers from any bacterial disease unless it be by production of protective substances in his own body.

The power within the body of resistance of body fluid and cells, when especially marked against any given type, we call immunity, and the converse term, susceptibility. Birds, for example, have a natural immunity against tetanus. We seem to have a heritage of acquired immunity from ages of vaccinating against smallpox and

the disease is now far less virulent. Centuries ago, in China and India, many people were inoculated for smallpox. This form of vaccination, after being lost for hundreds of years, was carried on again by the brilliant work of Jenner. In working with chicken cholera, Pasteur accidentally discovered that vaccination was efficient in conditions other than smallpox. Extension of this plan of treatment then became rapid, and it is now in general use, protecting human beings against a number of diseases. It is also in demand in animal husbandry. Pasteur made a study of germs concerned in fermentation and decay, showing methods of inhibiting their destructive processes as well as of destroying the micro-organisms. The destructive effects of their activities on living tissues were recognized by Lister, and he applied Pasteur's principles of the destruction of germs to the treatment of wounds and to operations performed in the surgical theater and thus developed antiseptic surgery.

Antibodies are developed in the serums by dead or attenuated living micro-organisms. The blood itself can be destroyed by certain of them. Antigen is the term applied to the substance which produces antibodies. The reactions occur between bacteria or their products and the body fluids.

Metchnikoff and his pupils have developed our knowledge of the cellular elements of the body as concerned in resistance to infectious germs. Phagocytosis or cell digestion is limited to certain of the white blood-cells, some endothelial cells, and giant-cells. Leukocytosis represents the increased number of the polymorphonuclear or digestive cells, as compared with the normal number; its amount depends on the reaction or the degree of infection. Metchnikoff believes these cells to be the cardinal factors in repair and that the antigen substance in the fluids which is destructive to bacteria is derived from the leukocyte. He also believes that the antigens armed the leukocytes for their work, thus differing from Pfeiffer, who believes that immunity lies in the fluids of the body. Wright, on the other hand, showed that the antibodies disarm the bacteria. In a study of the resistance of the blood, Wright and Douglas discovered a material which they named opsonin, which



removes the protecting albuminous covering around bacteria and makes them accessible and desirable as food for the phagocytes. Vaccines and serums do not accomplish the mechanical destruction of bacteria, nor can we put anything into the blood of a so-called antiseptic nature which will do so. They act only by raising the opsonic index, thus aiding yet leaving the blood to fight its own battles. Hektoen has done much original work in the support of Wright's views. Goadby shows that the opsonins wear out through repeated doses of bacteria and the immunity or resistance becomes decreased or broken down. In some cases the tissues become hypersensitized to certain infections, a form of anaphylaxis in which accumulated deposits of micro-organisms or their toxins, not necessarily pyogenic, but from local foci, are delivered into the body at intervals and for varying periods. In this group with known causes eventually may be placed such recurring diseases as urticaria, asthma, hay-fever, and so forth.

Wright's vaccines, prepared from bacterial cultures taken from the patient himself, have become of universal application in raising the resistance of the individual against the bacteria from which he suffers. Many bacteria grow well in mixed cultures and some are only thus rendered virulent. Vaccines in such cases must be made from combined organisms and not from pure cultures.

In the past the study of the body was looked upon as too sacred a thing to be freely considered by the people: the supposed benefits of medical aid were more or less closely allied with religion and were looked upon as rather mysterious.

The old family practitioner has almost entirely disappeared. In his day suppuration was one of the most common methods of wound-healing. He knew but little of microscopic examination and nothing of bacteria and protozoa. The examination of the blood, body secretions, and excretions was limited to the simplest possible tests. He therefore developed to a wonderful degree his powers of observation, now an almost lost art. The patient's facial expression, the eye, the skin, muscle tone, tendon twitching, circulation, and especially the condition of the mouth, tongue, gums, etc., were objects of his most careful observation. From such examinations

he could give almost as good a prognosis as the modern advanced methods of team diagnosis and prognosis are able to accomplish. It was before this period that Montaign said in regard to the ailment and its cure, whether it came about from the lapsing of a sufficient number of days, the remedies employed, the nature of the disease, or the grandmother's prayers, one could hardly say.

A great gain has come to mankind through the treatment of many diseases of which the specific germ cause is known, both by vaccines and the injection of the special prepared serums made from the blood of animals with a natural immunity to special micro-organisms. The years added to human life by diphtheria antitoxin alone are almost incalculable. From one of the most dreaded diseases diphtheria is now much less feared than many others—than scarlet fever, for instance, the infective agent for which is still to be found.

In obscure maladies and cases of puzzling diagnosis their immediate or past presence—however remote—in the system may in most cases, be determined by the reactions of the skin or of the blood in the body or in a test-tube in the presence of proper serums.

From the statements made it may appear that the treatment and cure of diseases caused by infection is rather a simple matter. This, however, is not the case, for while we are correct in theory, our practical work along these lines has not been sufficiently developed nor can it be successful in more than an average number of cases.

During recent decades the study of diseased conditions in the living body by properly controlled experimentation has shown remarkable results in the health and life of the human race. Much of this advancement is due to the practice of so-called preventive medicine. Up to this point we have progressed as far as post-mortem and pathologic findings would permit.

While today the great mass of our population have an extended general education, their information concerning disease and treatment comes largely from the advertising columns of our newspapers. This is a most serious mistake, and an ethical method of

rectifying it is now being put into operation through the Medical Lecture Bureau of the American Medical Association.

The prevention of disease today is one of the most important factors in the line of human endeavor. The Panama Canal has been made possible of accomplishment by the conversion of a pestiferous zone into one of remarkable health, a living record of the progress of science since the day of D'Lesseps and his French engineers, who failed in their efforts purely from a medical standpoint.

The difference between the knowledge of the layman and the medical attendant, including the dentist, should not be too great. Medical progress may be stayed from time to time that the layman may be educated to certain truths of health, that he may first know, then desire, and then demand proper health conditions. The public education by boards of health, school inspection, special committees and the medical profession have shown what can be done with that dreaded scourge, tuberculosis. All can appreciate the rapid change in health conditions along associated lines. Nineteen million dollars were spent during the last year in this country in public instruction and care of tuberculosis alone.

It falls upon the dentist and oral surgeon to study the diseased conditions of the mouth. Dental literature is full of it and much original work has been done by such leaders as Black, Talbot, Nodine, Hartzell, Brophy, and numerous others. The work is discouraging, but must be kept up, as eventually it will have its effect. The dentist's patients must be warned of the mouth as being by far the greatest portal of entrance of germ life into the body, *the most infected part of the alimentary canal*. The people will gradually demand more of their medical advisers. The next great step in medical progress in the line of preventive medicine should be made by the dentists. The question is, Will they do it?

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## DIPHTHERIA BACILLUS CARRIERS TREATED WITH CULTURES OF LACTIC ACID BACILLI\*

A. H. SANFORD

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There have been many forms of treatment suggested for ridding the throats of a "carrier" of diphtheria bacilli. At present the method much in favor is to attempt to crowd out the bacilli with a pure culture of *Staphylococcus pyogenes aureus*. That this can be done successfully is the testimony of many. There are complications to be feared, however. Instances of these are not usually reported in the literature, but there have been cases in which the pus-producers have been the cause of subsequent disorders—otitis media, for example. The writer suggests, therefore, the use of some harmless substitute for the pyogenic cocci, and at the same time to select an organism which is known to be a good antagonist to other bacteria. The *Bacillus acidi lactici* would seem to be the logical organism to use locally in the pharynx, as its power to fight the organism of the intestinal tract has been demonstrated.

Five cases have been treated recently in Rochester, Minn. (reported by Dr. H. B. Wood, of the Health Department of this city),† all of them giving negative cultures after a few days' spraying with cultures of *Bacillus acidi lactici*. This organism grows slowly on a solid medium, but after forty-eight hours there is usually sufficient growth on agar-agar slants to make a good suspension. The organisms are washed off with sterile normal salt

\* Reprinted from the Medical Review of Reviews, November, 1913, pp. 676, 677.

† Wood, H. B.: "Lactic-Acid Bacillus Spray for Diphtheria," Jour. Amer. Med. Assoc., August 9, 1913, vol. lxi, No. 6, pp. 392, 393.

solution and the cloudy fluid placed at once in a sterile atomizer. The living organisms are then sprayed in the pharynx and nasopharynx every few hours.

The first case in which this treatment was instituted was that of a cook at the Rochester State Hospital for Insane. Dr. Wood had been called to investigate and check what appeared to be a beginning epidemic of diphtheria among the patients and nurses. By culturing the throats of all the kitchen help it was found that this cook was a true carrier. She had not had symptoms of diphtheria, nor was she sick at any time. Her isolation checked the further spread of the disease. However, antitoxin, silver nitrate, phenol, and iodine failed to clear the throat of virulent organisms. At my suggestion a spray of living culture of *Bacillus acidi lactici* was tried, and followed at once by reports, from the State Board of Health, of negative cultures. No antiseptics were used in the throat in conjunction with the spray.

Four other patients were thus treated by Dr. Wood in May, 1913, with the same favorable results. Antiseptics were first used in these cases, but negative cultures were not obtained until the antiseptics were discontinued, and a spray of living organisms instituted. One of the cases was a very severe infection. In ten days 33,000 units of antitoxin were administered, and tincture of iodine used locally, with no disappearance of membrane. A marked decrease in the size of the membrane occurred thirty hours after beginning the use of the lactic-acid bacillus spray.

We have not tried the method in enough cases to give us any statistical evidence. However, the results in these few instances seem to warrant further trial, and it is with the thought that others may find the method efficacious that we are making this report. *Bacillus acidi lactici* is a harmless organism, and if it will crowd out *Bacillus diphtheriæ* in the throat, it would seem to be a better organism to employ in the treatment of diphtheria than *Staphylococcus pyogenes*.

# OBSERVATIONS ON PEPTIC ULCERS \*

CHRISTOPHER GRAHAM

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## INTRODUCTION

In this paper are presented notes on all cases of duodenal and gastric ulcers operated on in the Mayo Clinic during the years 1906 to 1911 inclusive; and our observations on diagnosis and statistics are based upon a study of the clinical records and operative findings.

It is often difficult, and it may be quite impossible, to differentiate clinically gastric and duodenal ulcers from other lesions causing gastric symptoms. It is often quite as difficult, and it may also be impossible, to locate the lesion in the stomach or duodenum if we have only the clinical picture to point the way. The symptoms of duodenal and gastric lesions may give exactly the same clinical picture, and for this reason we cannot at all times be definite when we attempt the localization of the ulcer. The radiogram gives the clinician great aid in these cases, and at times not only locates the lesion, but makes positive the diagnosis in some cases with irregular histories. However, the clinical history is still our greatest factor in the differentiation of lesions causing gastric disturbance, and we should consider it carefully in all its phases.

The various types of ulcers as observed in our clinic are almost wholly chronic in character, the acuteness or subacuteness depending more or less on acute exacerbations, *i. e.*, inflammation, infiltration, edema, or perforation.

In discussing the diagnostic features of duodenal and gastric ulcers we should consider, first, the periodicity of the attacks;

\* Read before the Kalamazoo Acad. of Med., December 9, 1913. Reprinted from Boston Med. and Surg. Jour., 1914, vol. clxx.

second, the chronic course; third, the significant symptoms that appear during the period of attack; and, fourth, the more or less ready control of symptoms, *e. g.*, pain.

1. *Periodicity of attacks* is almost constant in the duodenal and pyloric types of ulcers in which complications are not far advanced. When a patient presents himself with a history of attacks of gastric disturbance occurring day after day for several days or weeks, followed by remissions or intermissions of weeks or months of perfect health, one strongly suspects an ulcer. The onset of attacks often comes without apparent cause. However, close application to hard work, worry, anemia, exposure, and infection may be important contributing factors. During attacks the patient complains of pain, gas, sour regurgitations, and vomiting, coming regularly after meals, and more or less controlled by food. This identical picture is presented each day during the period of attack. Intermissions occur of complete relief for days, or, if the ulcer be situated high up, a remission may be experienced, if not a complete period of ease. These attacks and intermissions alternate for years with "spring and fall" influence often noted. They increase in frequency, number, and severity until the patient seeks relief in treatment. Such a history of periodicity is often quite enough in itself to warrant a probable diagnosis of ulcer.

2. *Chronicity*.—The patient rarely fails to emphasize the fact that these distressing symptoms have been coming and going for many years until finally he is forced to seek relief. The symptoms have remained the same in character, but have increased in length of period and intensity until some complication has arisen to disturb the characteristic course. In general the cases observed in our clinic have covered a course of many years,—few less than one,—the greater number falling between five and twenty years, the average being from eleven to twelve years. When we consider the average long series of years the symptoms have existed, with the distress always increasing, and, as years go by, with invalidism increasing and often becoming quite complete, it seems strange, not that so many patients have been urged to seek relief in surgery, but rather why surgical measures were not urged



earlier, at least on the appearance of symptoms indicating that the medical border-line had been passed. In our series this history of prolonged attack with intermission or remission covering years was clear in 85 per cent. of the cases, and is a factor to be taken into serious consideration.

3. *Pain*.—During the period of attack, pain is the most constant symptom (pain or distress, 95 per cent.), and it is characteristic in its manifestations. The location of the pain, its type, and its area of radiation are of secondary diagnostic significance: (a) because most pain is described as epigastric, regardless of the location of the lesion causing the gastric syndrome; (b) because the pain complained of varies from mild distress, burning, griping, or colic, to a severe type requiring opiates for relief; and (c) because radiation is not common in uncomplicated ulcers, and because, if a clear-cut, radiating pain to the back occurs, as in some posterior perforating ulcers, or if the radiation is to the lower abdomen, cholecystitis or appendicitis may be inferred. Thus our diagnosis may be clouded, rather than cleared, by the radiation.

4. *Time and Control of Pain*.—It is the *time* of pain and the *control* of pain that are characteristic and diagnostic. The time of its appearance, the time and manner of disappearance, and its control by food, alkalis, position, and rest (vacation), are quite conclusive evidences for a correct diagnosis. Pain appears after meals, or in clear-cut, duodenal types two hours before meals. It usually comes one-half to four hours after eating, depending in a measure on the location of the lesions. The nearer to the gastric outlet, the longer the period of food-ease is the rule. A burning, gnawing, painful feeling begins sooner or later after meals, following a definite type in each case, increasing in severity and continuing until the stomach empties and pain ceases before the time for the next meal, or continues up to meal-time. The early cessation of pain is noticed most often in the histories of ulcers occurring above the pylorus. The pain, beginning later (two to four hours), as in purely duodenal types, may continue until vomiting, irrigation, alkalis, or the next meal brings relief. Food

relieves pain, gas, and acidity in a large percentage of cases (76 per cent.). This relief lessens as the pathologic lesion extends, and in the late stages little or no ease comes from food. Indeed, when complications, such as perforations, adhesions, and obstruction, are far advanced, food usually gives immediate pain, and only forced vomiting and irrigation afford relief. Alkalis are less efficient at this time than in the earlier stage.

The pain and accompanying symptoms then appear in definite periods of attack. They come daily, often two or three times a day, at a definite time after ingestion of food, during the entire period of attack. The onset of symptoms varies from one-half to four hours after meals, and they are oftener pre-meal than after-meal. The pain is epigastric, seldom radiating to other areas, and, except in the later stages, is relieved in part or fully by food, drink, alkalis, vomiting, or irrigation.

What, then, are the typical diagnostic symptoms of peptic ulcer? (1) The period of attacks and perfect intermission or marked remission of attacks; (2) the almost exact similarity of symptoms occurring for days during the period; (3) the marked relation of symptoms to food intake (one-half to four hours); (4) the control of symptoms by food, alkalis, lavage, posture, and rest.

The types of cases in which it is particularly difficult to reach a correct diagnosis, or in which it is quite impossible to differentiate from other lesions causing gastric symptoms, may be divided into four groups:

GROUP I: This group comprises those patients with ulcers who give the classic symptoms of gall-stones, and in whom no other gastric symptom can be elicited. In this group there may be perforations, or the pain may be due to acidity and accompanying spasm. The lesions are usually chronic and may be located at any point in the stomach or duodenum. At operation, perforation has been found in about one-third of this group (35 per cent. duodenal; 29 per cent. gastric), and in some of these, at least, the pain has not been more intense than in those not found perforated at operation. Severe pain may be complained of and no perforation be evident. Patients with this symptom-complex constitute

about 5 per cent. of all the cases. In them the diagnosis of gall-stones is the only logical one to be made. Careful clinical research and radiography should lessen our errors.

GROUP II: In this group may be found patients in whom the ulcer must have been latent for weeks or months, and whose first manifest symptoms were those of chronic ulcer with complications (hemorrhage, perforation, etc.). The symptom-complex in these cases is irregular, and quite excludes the pathognomonic picture of ulcer.

GROUP III: In these cases the present chronic symptoms are very severe. The early symptoms were so mild that they may have been quite forgotten or overlooked by the patient. Many such patients will not allude to the early trouble unless carefully questioned, because nothing is of so much importance to them as the present or recent years of distressing pain.

GROUP IV: In the fourth group are those patients whose symptoms are of a more or less malignant type—marked loss of flesh and strength, pain or distress quite continuous, gas rather annoying, and vomiting of large amounts at irregular periods. The vomitus consists of food, fairly macerated, perhaps dark, coffee-ground color, and the liquid quantity quite in excess of fluid ingested. If to these symptoms is added the presence of tumor, we are inclined to err in diagnosis and consider cancer first. Three per cent. of all ulcers in this series were diagnosed cancer; 5 per cent. had gross tumors; 3 per cent., more or less the “feel” of a ridge.

The cases in these groups may be variously diagnosed as acute or chronic gall-stone disease, gastric ulcer, chronic appendicitis, tuberculous intestinal involvement, or cancer, in accordance with the variation of the symptoms. Here, too, by a more careful attention to clinical histories and more frequent use of the Roentgen-ray, we should materially lessen our errors.

In diagnosing atypical cases, one should take into consideration the variations in symptoms. The following groups suggest themselves: (1) Those cases of a clear-cut gall-stone type. (2) Those which have been chronic and complicated since the first symptoms appeared, *i. e.*, chronic ulcers long latent. (3) Those in which the

ulcer is high on the gastric wall and tends to continuous symptoms without food ease; and (4) cardiac ulcer, usually with but slight symptoms until obstruction appears. However, the general picture is so clear that 80 per cent. of all ulcers may be followed closely enough to establish an accurate clinical diagnosis, and a probable diagnosis may be consistently made in the remainder.

Ulcers of the duodenum and pyloric area without complications are usually so clear-cut in their symptomatology that they may be diagnosed with little trouble. Ulcers located higher up may simulate the duodenal type closely and be thus diagnosed, or they may vary in symptomatology just enough to be atypical, yet be clearly gastric.

Other things being equal, the histories of uncomplicated types of duodenal and pyloric ulcers are clean-cut throughout the entire symptomatology. The longer the period between food-intake and onset of symptoms, the lower the ulcer, as a rule. The more prompt the food ease and cessation of symptoms, the lower the ulcer. In ulcer of the stomach proper, the attacks are not so clear-cut as in duodenal and pyloric types, nor are the day-by-day symptoms so clearly defined. In those well above the pylorus the symptoms are apt to be continuous for longer periods, or remissions rather than free intervals are apt to be noted. These symptoms are not so often eased by food, or small amounts of food may give relief while increased food may give distress. More care in diet is necessary. Soda relieves when food does not. Pain begins earlier, as a rule, oftentimes disappearing before the next meal, and thus the food relief feature is minimized, but pain one-half to one hour after food is quite the rule, and is of great diagnostic significance.

A gnawing sensation coming regularly when the stomach is empty is almost "hunger pain." In such instances the effect of food may be translated as distress-producing, though it relieves the gnawing. Radiation of pain and the area of complaint are considerably more extensive in gastric than in duodenal types.

Vomiting in gastric ulcer is rather more common than in ulcers of the duodenum and pylorus, unless complications, *e. g.*, obstruc-

tion, are present. Also vomitus containing food is more apt to come sooner, hence it is not in so advanced a stage of digestion. Blood is more frequent in the vomitus of cases of the gastric type.

In those conditions which oftenest cloud the diagnosis, such as chronic gall-stones, chronic appendicitis, etc., we obtain our greatest diagnostic aid from the wide irregularity of symptoms during the period of attack. Yesterday's pain came before meals; today's pain after meals; tomorrow's pain an all-day "miserable feeling." Food-ease yesterday because fasting the previous day; today food pain wholly reflex; vomiting one day and gas another; yesterday well, today in the depths mentally. Nothing follows in sequence day by day, because the stomach behaves properly unless irritated by the distant lesion, and this extrinsic lesion is irregular in its influence. The stomach then delivers what symptom it may when the irritation is great enough.

If attacks of "indigestion" occur which are not quite clear-cut; if during the attack there is some lack of regularity of symptoms; if the pain be somewhat continuous; if remissions, even, are not marked; if, together with the gastric symptoms of distress, gas, bloating, sour regurgitations, or vomiting, continuing for a few days, to longer periods; and if each day the symptoms quite nearly repeat those of the day before; if *some* relation to food be observed; if the symptoms come on one-half to one hour or more after meals; if alkali or irrigation gives relief—if these conditions prevail, we may safely exclude from the diagnosis everything but peptic ulcer. Added to this, if we obtain a history of partial and fairly constant food relief, we may be quite sure of our diagnosis. In locating the ulcer, one may be aided by the field of radiation, as when it is high and well to left, or when there is perforation at any point. The patient's interpretation of pain and of the field of radiation is often perplexing. Localization by means of tender abdominal pressure-points is not wholly satisfactory, partly perhaps because of the varying positions of the stomach. The Roentgen-ray helps in many perplexing cases, and promises even greater aid in the near future.

However, the greatest benefit to be derived from a diagnosis does not come from exact localization of the ulcer, but rather from the diagnosis of a lesion, and determining the patient's needs as to treatment, in the light of the available symptoms. Whether or not a patient be advised to undergo medical or surgical treatment often depends upon our point of view and is a theme for discussion by itself. Cases complicated with obstruction, hour-glass contraction, perforation, and hemorrhage are conceded as being surgical. Patients suffering from oft-repeated or continuous attacks, and whose *usefulness* or *pleasure* in life is greatly diminished thereby, certainly should be given the relief afforded by surgery, even though the above complications are not present.

#### STATISTICS

The following statistics are based on the reports received from 600 cases of duodenal and gastric ulcer out of a total of 816. The shortest period since operation in these cases is now nearly two years.

Of all the patients with ulcer operated on during the years 1906-11 inclusive, 76 per cent. were males and 24 per cent. were females. Of the males, 70 per cent. of all ulcers were duodenal or involved the duodenum. Of the females, 60 per cent. of all ulcers were duodenal or involved the duodenum.

Out of a total of 567 cases of duodenal ulcer operated on during a period of six years (1906 to 1911 inclusive), information has been received concerning 438. The classified results of these data are as follows: 307, or 70 per cent., cured; 79, or 18 per cent., much improved; 40, or 9 per cent., fair; and 12, or 3 per cent., unimproved. A percentage, therefore, of 88 were cured or much improved. In 440 of the cases the ulcer was confined to the duodenum. Of these, 337 were heard from: 70 per cent. were cured; 16 per cent. much improved; 11 per cent. fair, and 3 per cent. not improved. In the remaining 127 cases the ulcer extended to or involved the pylorus, and of these, 72 per cent. were cured; 24 per cent. much improved; 3 per cent. fair; and 1 per cent. unim-

proved. That is, 86 per cent. of the former were cured or had made satisfactory improvement, whereas in the latter group, in which the lesion was more extensive, 96 per cent. were cured or much improved. The results are summarized in the following table:

TABLE I

ULCER	NUM- BER OPER- ATED ON	NUMBER REPORT- ING	CURED	MUCH IMPROVED	FAIR	NOT IMPROVED	CURED AND MUCH IMPROVED
			Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Duodenum.....	440	337	70	16	11	3	86
Duodenum involv- ing pylorus.....	127	101	72	24	3	1	96
Total averages.....	567	438	70	18	10	2	88

There were 249 cases of gastric ulcer, and reports were received from 162. These were grouped according to their situation: (1) 52 in or at the pylorus (pyloric ulcer), and (2) 197 in other parts of the stomach (principally the lesser curvature). Taken collectively, 95, or 59 per cent. of this series, were cured; 35, or 22 per cent., were much improved; 21, or 13 per cent., fair improvement, and 11, or 7 per cent., unimproved. Therefore, 80 per cent. were either cured or much improved, 93 per cent. were benefited, and 7 per cent. not improved. Tables II and III show comparative results in this series.

TABLE II

ULCER	NUM- BER OPER- ATED ON	NUMBER REPORT- ING	CURED	MUCH IM- PROVED	FAIR	NOT IM- PROVED	CURED AND MUCH IM- PROVED	BENE- FITED
			Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Pyloric.....	52	37	51	27	19	3	78	97
Gastric.....	197	125	61	20	11	8	81	92
Total average.....	249	162	58	22	13	7	80	93

TABLE III.—COMBINED RESULTS

ULCER	NUM- BER OPER- ATED ON	NUMBER REPORT- ING	CURED	MUCH IM- PROVED	FAIR	NOT IM- PROVED	CURED AND MUCH IM- PROVED	BENE- FITTED
			Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Duodenum.....	567	438	70	18	9	3	88	97
Gastric.....	249	162	58	22	13	7	80	93
Total average.....	816	600	67	19	10	4	86	96

Clinical observation goes to prove that the more advanced the obstruction at the pyloric end of the stomach, other things being equal, the better is the result following gastrojejunostomy, and, conversely, it is equally true that those cases with slight or no obstruction are to some degree less benefited by the operation. In the latter instance this result has been explained on the theory that the pylorus remains open and a portion of the food, with its irritating, though perhaps normal acids, continues to pass by way of the natural channel coming in contact with the ulcer as before, thus giving a lessened opportunity for the ulcer to heal. This condition of free passage of gastric content by the natural route has been repeatedly verified by postoperative screen and Roentgen-plate study, yet many patients whose stomachs are thus functioning are, nevertheless, without symptoms. It is, however, because of this failure to relieve all patients that the surgeon has undertaken various procedures to overcome this difficulty, among which are excision or infolding of the ulcer, infolding the pyloric end of the stomach, ligation by means of silver wire or twine, and, more recently, the employment of a ligature of live tissue of fascia or omentum, none of which methods has been signally successful.

Pyloric obstruction to a variable degree occurred in 198, or 34 per cent., of the 576 cases of duodenal ulcer. Gastric analysis showed food remnants in varying amounts after twelve hours in 100 cases, or 50 per cent. Reports were received from 163 patients.



Nine had died since the operation. Ninety-four per cent. of the remainder were cured or greatly improved.

In 197 of the cases of gastric ulcer obstruction was present in 78, or 39 per cent. Food remnants were noted in 58, or 71 per cent. Thirteen patients had died since the operation. Ninety-two per cent. of the remainder were cured or greatly improved. The results in these two series (Table IV) are encouraging in view of the fact that some complication, such as chronic or subacute perforation, regional peritonitis and adhesions, multiple ulcers or coincident disease in the gall-bladder or appendix, or both, were frequently noted at the operation.

TABLE IV.—PYLORIC OBSTRUCTION

ULCER	NUM- BER OPER- ATED ON	NUM- BER RE- PORTED	FOOD REM- NANTS	CURED	MUCH IM- PROVED	CURED AND IM- PROVED	FAIR	NOT IM- PROVED	COM- PLICA- TION	OTHER OPERA- TIONS
			Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Duodenum . .	198	163	25	71	23	94	3	3	40	18
Stomach . . .	78	52	71	67	25	92	6	2	43	7

The number of duodenal ulcers without evidence of obstruction either clinically or at operation was 275. The results were classified as follows: Cured, 68 per cent.; much improved, 17 per cent.; fair, 12 per cent.; not improved, 3 per cent.; cured and improved, 85 per cent.; total number benefited by the operation, 97 per cent.

TABLE V.—DUODENAL ULCERS WITHOUT OBSTRUCTION

NUMBER REPORTED	CURED	MUCH IMPROVED	FAIR	NOT IMPROVED	CURED AND IMPROVED	BENEFITED
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
275	68	17	12	3	85	97

Of 162 gastric ulcers, there were 110 without evidence of pyloric stenosis. The results were classified as: Cured, 51 per cent.; much improved, 23 per cent.; fair, 14 per cent.; not improved,

12 per cent.; cured and improved, 74 per cent.; total number benefited by the operation, 88 per cent.

TABLE VI.—GASTRIC ULCER WITHOUT OBSTRUCTION

NUMBER REPORTED	CURED	MUCH IMPROVED	FAIR	NOT IMPROVED	CURED AND IMPROVED	BENEFITED
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
110	51	23	14	12	74	88

TABLE VII.—SUMMARY

ULCER	NUMBER	CURED	MUCH IMPROVED	FAIR	CURED AND IMPROVED	BENEFITED
		Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Total duodenal.....	438	70	18	10	88	98
Duodenal (obstructed) .	163	71	23	3	94	97
Duodenal (no obstruction) .....	275	68	17	12	85	97
Total gastric.....	162	58	22	13	80	93
Gastric (obstructed) ...	52	67	25	6	92	98
Gastric (no obstruction) ...	110	51	23	14	74	88

By a comparison of the results obtained (see Table VII) it will be noted that the percentage of cured and improved cases of duodenal ulcer with obstruction was 94 per cent.; without obstruction, 85 per cent.; making a difference of 9 per cent. The number of cured and improved cases of gastric ulcer with obstruction was 92 per cent., and without obstruction, 74 per cent., a difference of 18 per cent. The comparatively good end-results in these cases of duodenal ulcer without obstruction may be explained on the theory that: (1) The ulcer in healing contracts and causes partial or complete pyloric or duodenal stenosis. However, the end-results in gastric ulcers without obstruction are so successful that the clinician need not delay his surgical diagnosis until obstruction or other serious complication endangers the patient. (2) In about 50 per cent. of the cases classified as obstructed the degree of obstruction was only moderate, and from a practical standpoint the end-results between these and the unobstructed

cases should be very similar. (3) Undoubtedly the reflux of bile and pancreatic secretion from the duodenum into the stomach, with its strong neutralizing action upon the hyperacid gastric contents, favors healing of the ulcer and consequent remission of all symptoms.

It may be that the improved drainage better defends the duodenum and pylorus, on account of their situation, from the irritating gastric content, or, as a result of the operation, the acid irritation is lost to the duodenal and pyloric areas. Thus in this location healing is hastened. Ingested matter and acidity may still irritate the ulcer higher up (cardiac end).

TABLE VIII.—DUODENAL ULCER. POST-OPERATIVE SYMPTOMS: DEGREE OF IMPROVEMENT

SYMPTOMS	INFLUENCE OF FOOD					HEMOR- RHAGE	LOSS WEIGHT	GAIN WEIGHT	CON- STI- PA- TION
	Pain Eased	Dis- tress and Pain	No Effect or Agrees	Vom- iting	Gas				
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Before operation . .	76	16	9	70	80	19	70		58
After operation . .	3	17	80	13	18	7	10	68	8

In the series of duodenal ulcers 106, or 19 per cent., of patients gave a history of hemorrhage preceding operation. Thirty-one patients had hemorrhage of variable degree following the operation, but only 18 of these had hemorrhage prior to operation. Therefore there was hemorrhage in 13 cases following operation in which there was no history of preoperative bleeding. In these the hemorrhage occurred some time after operation, and was severe in only a small percentage. Out of a total of 108 patients, 94, or 88 per cent., had a gastro-jejunostomy performed only; 4 per cent. had excision or infolding of the ulcer in addition to the gastro-jejunostomy. Excision or pyloroplasty was done in 8 cases, or 8 per cent. Three of the patients had postoperative hemorrhage in which excision or infolding had been done.

TABLE IX.—GASTRIC ULCER. POSTOPERATIVE SYMPTOMS: DEGREE OF IMPROVEMENT

SYMPTOMS	INFLUENCE OF FOOD					HEM-OR-RHAGE	LOSS WEIGHT	GAIN WEIGHT	CON-STI-PATION
	Pain Eased	Dis-tress and Pain	No Effect or Agrees	Vom-iting	Gas				
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Before operation . . . . .	60	30	11	71	81	23	73	..	62
After operation . . . . .	1	23	76	19	20	6	12	61	15

Forty-eight, or 23 per cent., of the patients with gastric ulcer had hemorrhage prior to operation. Eight patients, or 13 per cent., had postoperative hemorrhage, and of this group only three gave a history of hemorrhage prior to operation. Thus in 5 instances there was bleeding in varying amounts following operation in which there was no preoperative history of hemorrhage. Gastro-jejunostomy alone was done in 44 per cent.; jejunostomy and excision or infolding of the ulcer, in 80 per cent. Excision alone, pyloroplasty, or resection, with or without gastro-jejunostomy, was the operation of choice in 48 per cent. Gastro-jejunostomy alone was effective in preventing recurrence of hemorrhage after operation in about 60 per cent. of all cases which gave a history of hemorrhage prior to operation. Hemorrhage may follow operation in a small percentage of cases, even when an effort has been made to prevent recurring hemorrhage by excision, infolding, or ligation of vessels leading into the ulcer. In all cases in which there is a history of repeated hemorrhage effort should be made to control future bleeding by whatever technic is feasible.

TABLE X.—TOTAL POST-OPERATIVE RESULTS

NUMBER LETTERS SENT	ANSWERS RECEIVED	FOOD INFLUENCE ON SYMPTOMS					OTHER SYMPTOMS					ACIDITY	NERVOUSNESS	MOTILITY
		Eased	Distress	No Effect or Agrees	Vomiting	Gas	Hemor-rhage	Weight Loss	Weight Gain	Average Gain	Constipation			
		Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Lbs.	Per Cent.	Per Cent.	Per Cent.	
773	600	2	20	78	15	17	6	11	65	25	9	10	6	1.2

*Postoperative Results.*—Among other things, our inquiries as to the postoperative condition of the patient were directed to the influence of food upon such symptoms as pain, distress, vomiting, and gas. It is noted (Tables VIII, IX, X) that before operation control of pain by food was a great factor. It also controlled other symptoms. After operation there was little necessity for such control. The greatest benefit, according to our statistics, was that, following operation, food could be well borne without producing untoward symptoms, and that pain, vomiting, and gas were markedly relieved. There was a gain in weight in 65 to 75 per cent. of the cases and constipation was greatly reduced. The most marked postoperative symptoms generally followed in those instances of chronic or subacute perforation of the ulcer in young adults. In these cases the acidity and hypersecretion were especially marked and peristalsis active.

The coexistence of disease in the appendix (16 per cent.) or gall-bladder (7 per cent.) was noted and corrected in 11 per cent. of all the cases of duodenal ulcer. In the group of gastric ulcers coincident disease of the appendix (14 per cent.) or gall-bladder (5 per cent.) was present in 9 per cent. In a considerable number of cases operation was necessary on both organs in addition to the ulcer, with favorable end-results.

Actual recurrence of an ulcer following a properly performed gastrojejunostomy is infrequent,\* but it has recurred, in a few instances, when there was no obstruction of the pylorus at the time of the primary operation. In another small group a secondary operation was necessary, owing to the formation of a "new ulcer at the site where the gastrojejunostomy was made, due to heavy silk or linen hanging in the suture line of the gastrojejunostomy."

The patient who seeks relief from distressing symptoms cannot always appreciate a "practical" cure. To cure is relative, and depends on various conditions: (1) General nervous stability; (2) the pathologic condition present; (3) the extent of this condition; (4) the proximity of the lesion to vital tissues; (5) extent

\* W. J. Mayo: "Recurrence of Ulcer of the Duodenum Following Operation," Boston Medical and Surgical Journal, 1914, vol. clxx.

of operation necessary to remove the diseased tissue; (6) coincident diseases; (7) the patient's power to react. These factors enter into consideration when treatment, especially surgical, is to be instituted. The patient may be, and often is, freed from disease and life prolonged; yet he may not be freed from symptoms quite distressing. This is not always the fault of treatment, but an inevitable result of the pathologic condition occurring before treatment was undertaken.

# DIAGNOSTIC VALUE OF BLOOD OR HEMORRHAGE IN GASTRIC AND INTESTINAL LESIONS. CLINICAL AND STATISTICAL STUDY \*

GEORGE B. EUSTERMAN

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The object of this study was undertaken largely to determine the diagnostic value of bleeding in lesions of the stomach, duodenum, gall-bladder, and appendix, which have been operated on. Repeated hemorrhage in the presence of a preceding history of epigastric pain, distress, and gastric disturbance signifies an ulcer of the duodenum or stomach in over 90 per cent. of the cases.<sup>1</sup> As regards occult blood-findings in the gastric or stool analyses, the conclusions to be drawn therefrom must depend largely on associated clinical symptoms, owing to the delicacy of the chemical tests, because such factors as trauma and food retention are instrumental in giving positive reactions.

Occult blood tests are of undisputed value in the differential diagnosis of doubtful cases. In those cases undergoing medical observation and treatment the internist estimates the duration of active treatment from the time of the entire disappearance of blood from the stool, or advises surgical measures if gastric and stool reactions persist positive or increase in spite of all attempts at healing. Until recently routine examination of three and four day meat-free stools in suspected cases of ulcer have not been made, inasmuch as other data, perhaps more reliable, have invariably been present in helping to establish the diagnosis.

Simple chronic ulcer of the stomach or duodenum bleeds only intermittently and, owing to the brief space of time that the

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average patient comes under observation prior to the operation, routine examination of the stool for occult blood should have a restricted value except in those cases where the diagnosis is questionable. The results of the examination of the feces for occult blood are often unreliable, owing to the possibility of bleeding areas from any point between the lips and anus, thus giving positive blood or pigment reactions, the degree of reaction depending on the sensitiveness of the reagent employed.

In cancer the conditions are quite the contrary, owing to the continuous seepage of blood from the affected area, a fact which applies to cancer of all the other mucous surfaces. The gastric analyses of 688 recent consecutive cases of gastric cancer showed altered blood findings in 75 per cent. In these cases blood is found quite regularly in the stools, various well-known authorities finding it constantly present in 80, or 90 per cent. Therefore, the value of the examination of the feces in doubtful cases is self-evident.

During the review of the material herewith presented, in any instance where there was a reasonable doubt as to actual hemorrhage, or source of blood other than the stomach or duodenum, such cases were rejected in the final analysis. Often in the cases of hemoptysis or epistaxis from whatever cause, blood may be swallowed, then regurgitated or vomited; or, as occasionally happens, the patient has partaken of cranberries, red wines, cherries, red sausage, chocolate, etc., prior to vomiting; and in this way has led himself to believe or convinces the physician that blood has been vomited.

Pseudohematemesis or melena may be associated with various preparations of bismuth or of iron. Other rarer factors are hemoptysis of pulmonary or cardiac disease associated with lung infarct, the irritation produced by trauma, poisons, emetics, purgatives, etc.

Indirect local causes of bleeding are portal obstruction in cirrhosis of the liver, syphilis of the liver, portal thrombosis (80 per cent. esophageal), and splenic enlargement as in splenic anemia. (In our series of 18 operative cases hematemesis in



considerable degree occurred in 5, or 28 per cent.) There are general causes in which hemorrhage occurs from various mucous membranes as well as from the gastric, *e. g.*, sepsis, the exanthemas, autotoxic states, cholemia, and uremia, blood dyscrasias and diseases, such as hemophilia, purpura, scurvy, the leukemias, and pernicious anemia. Hemorrhage may be incident to various neuropathies, vicarious menstruation, and burns. Occasionally a single hemorrhage, moderate to profuse, is experienced, the origin or causation of which may always remain undetermined. In a very small percentage of duodenal and gastric ulcers a profuse or even alarming hemorrhage may be the first evidence of their presence. Neuropathic hematemesis, a condition described by some writers, is usually seen in neurotic individuals, in whom the hemorrhage may recur, is never fatal, the nutrition remains unimpaired, and the patient does not seem concerned about the bleeding. But even in these instances the probability of an ulcer must be considered.

#### HEMORRHAGE IN CHRONIC DUODENAL AND GASTRIC ULCER

The incidence of gross bleeding in these cases is much more infrequent than is commonly supposed, and one could easily agree with Moynihan that hemorrhage should be looked upon as a complication, rather than as a part of the symptom-complex. This infrequency is explained or borne out by the fact that at the operation the base of the ulcer is seen to be clean and free from granulation tissue. This feature is of clinical importance since the diagnosis of chronic simple ulcer of the duodenum or stomach must usually be made in the absence of hemorrhage, which occurs in approximately less than one-fourth of all cases.

In 568 duodenal ulcers which have been operated on a history of hemorrhage by mouth was recorded in 94, or 16.5 per cent., and by bowel in 18, or 3 per cent. In 127 of these cases the pylorus was involved. In the 94 cases of hematemesis (16.5 per cent.) blood had been noted in the stools in 73 (14 per cent.). In 249 cases of gastric ulcer there was hemorrhage by mouth in 54 (22 per cent.) and by bowel in 4 (2 per cent.). In these 54 cases blood in the stools was noted 42 times. In a total of 817 cases an

average of 20 per cent. gave evidence of gross bleeding from the stomach or bowel or both. In the 497 analyses of gastric contents in this group (568), occult blood was found in varying degree in 17 per cent. In the 249 cases of gastric ulcer blood was present in 20 per cent. In considering these latter statistics it is to be remembered that the test-meal analyses were rarely made more than once, and in some of the duodenal cases not at all. The results in the stool examinations are withheld until a larger series can be reported.

#### HEMORRHAGE IN DISEASE OF THE GALL-BLADDER

These cases form an interesting group clinically, because when gastrorrhagia, melena, and positive occult blood findings do obtain, error in diagnosis is common. Even in the absence of bleeding, mistakes are made in the differential diagnosis between lesions of the gall-bladder and stomach in about 10 per cent. of cases. This is often true regardless of careful case histories, gastric analyses, repeated physical examination, and, if necessary, the use of the fluoroscope and Roentgen-ray.

In reviewing the records of this series of cases one is impressed with the frequency of reflex gastric disturbances, namely, epigastric pain after food, flatulence, hyperacidity, nausea, vomiting, and other symptoms which closely simulate ulcer, and which can probably all be explained by the resulting pylorospasm, gastritis, and secretory perversion within the stomach. In 46 per cent. of the 500 cases studied, gastric analyses were made largely on account of the marked gastric features present. But in a major percentage of these cases the dyspepsia was usually continuous, irregular as to food relation, occurred frequently in young individuals, nutritional disturbances were not so marked, and, finally, that chronicity and periodicity, usually so characteristic of ulcer, were absent. Moreover, other evidences suggesting disease of the gall-bladder were occasionally present, such as acute localized pain or tenderness at some time in the course of the disease, icterus perhaps, chilliness and fever, and antecedent typhoid infection.

Two hundred and fifty consecutive cases each of chronic cholecystitis and cholelithiasis were considered in this series.

Although a much larger amount of material was available and might be preferred, the findings in these cases should furnish a fair blood index, so to speak. Profuse bleeding occurred but rarely, although small amounts of blood were vomited or passed in the stool in 2 to 4 per cent. of the cases. One patient in this series having gall-stones had copious vomiting and melena following an acute painful seizure. Another patient gave a history of profuse vomiting of blood mixed with pus, and operation revealed the fact that gall-stones had perforated into the stomach just above the pylorus. In the cases of chronic cholecystitis three patients in the series vomited over a pint or more, one of whom fainted. Copious bleeding did not recur in these cases, unlike the hemorrhage in duodenal or gastric ulcer.

The pathologic findings in the cases having hemorrhage showed a marked septic process in the gall-bladder, in all instances requiring a cholecystectomy. The association of lesions in the duodenum or stomach and gall-bladder is not at all uncommon, but a systematic exploration of the former organs was negative for ulcer and satisfactory post-operative recovery followed.

In this series of cases it is of interest to note that in the 228 instances in which gastric analyses were made, 98, or 43 per cent., showed positive altered blood findings, and of the entire series (500), 20 per cent. showed positive altered blood findings. This fact, in conjunction with evidence of gross bleeding and suggestive gastric disturbances, may explain the primary or alternative diagnosis of gastric ulcer. Bleeding in this group in the absence of any demonstrable ulcer can only be explained in the light of our present knowledge, first, by mechanical trauma to gastric mucosa and arterioles the result of retching, and second, by a toxemic result in the stomach or duodenum dependent on a continuous septic process in the gall-bladder in which waves of a more acute infection may from time to time occur, provoking the so-called gastrototoxic hemorrhage.

#### BLOOD IN DISEASE OF THE APPENDIX

In 500 consecutive cases of chronic and subacute appendicitis there was no instance of serious hemorrhage. In three cases there

was hematemesis in small amounts. In eight there was blood in the stool, and in two of these pus was mixed with the blood; all had more or less intestinal irritation simulating colitis. In one instance where there was a definite amount of blood vomited and passed in the stool gastric disturbances were marked from the outset, and everything considered, strongly suggested an ulcer. On exploration of the stomach it was found negative and a subacutely inflamed retrocecal appendix was removed. There was, however, a band of adhesions, extending from the mesocolon, which had slightly constricted the pylorus. These were regarded as congenital. In 110 test-meal examinations altered blood was present to a variable degree in 26, or 24 per cent., or in 5 per cent. of the entire series.

There may be several points of interest with respect to disease of the appendix in its relation to hematemesis and to other abdominal lesions, particularly of the stomach and duodenum. In our experience there have been instances of hematemesis more pronounced than have been evidenced in this series of cases. Recent literature expresses the opinion in one way or another that a primary focus of infection within the abdomen is responsible for the later, strictly secondary, and dependent lesions which we recognize as acute ulceration, erosion, fissure, and, finally, chronic ulceration in the stomach and duodenum. The appendix is the more frequent source of such infections. Aside from facts obtained experimentally and clinically, it is a common surgical experience to find advanced disease of the appendix as evidence of old inflammatory processes in that organ associated with lesions of the gall-bladder, pancreas, stomach, or duodenum. Finally, fatal hematemesis following appendectomy has often been reported. Hutchinson, at the London Hospital, records 24 fatal cases of post-operative hemorrhage from the stomach. Of these 24, no fewer than 21 were cases of appendicitis with septic complications, localized abscesses, or diffuse peritonitis. In 3 cases recent acute ulcers were found in the stomach (twice) and in the duodenum (once); in the remaining cases, only "hemorrhagic erosions" were found. These facts show clearly how dependent a severe hemat-

emesis may be upon lesions not primarily connected with the stomach.

#### CONCLUSIONS

Repeated hemorrhage in the presence of a preceding history of gastric disturbances with pain or distress signifies an ulcer of the duodenum or stomach in more than 90 per cent. of the cases.

Examination of the gastric contents and meat-free stool for occult blood is of undisputed value in the differential diagnosis of doubtful cases, and in estimating the effectiveness and duration of dietetic and medicinal treatment. However, positive occult blood findings, unless taken in conjunction with the clinical symptoms and physical findings, may lead to wrong conclusions.

In 568 proved cases of duodenal ulcer single or repeated hemorrhage, by mouth or bowel or both, occurred in 19½ per cent.; in 249 cases of gastric ulcer in 23 per cent. In disease of the gall-bladder gross bleeding in variable amount occurred in 2 to 4 per cent.; in chronic and subacute appendicitis in 1 to 2 per cent.

Positive occult or altered blood findings, in order of frequency, are incident to gastric cancer, chronic simple ulcer of the duodenum and stomach, disease of the gall-bladder and appendix. Altered blood was present in the gastric extracts in 75 per cent. of 688 cases of gastric cancer, in 17 per cent. of 497 gastric analyses, in 568 cases of duodenal ulcer, and in a general average of 28 per cent. in 343 cases of gastric ulcer. In 228 analyses of 500 gall-bladder cases positive occult blood reactions were obtained in 43 per cent., or in 19.6 per cent. of the total (tincture of guaiac or benzidin tests). In 110 analyses of 500 cases of appendicitis a positive reaction with similar reagents was present in 24 per cent., or in 5.4 per cent. of the total.

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# INCIDENCE AND DIAGNOSIS OF COMPLICATING FACTORS IN GASTRIC AND DUODENAL LESIONS. RESULTS IN 1800 CASES OPERATED ON \*

GEORGE B. EUSTERMAN

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The material for the following study was obtained from cases operated on in the Mayo Clinic from 1906 to 1912 inclusive, and consists of 778 cases of duodenal ulcers, 324 cases of gastric ulcers, and 691 cases of gastric cancer. Only the more frequent and important complications or sequelæ are considered, *i. e.*, pyloric obstruction, perforation, hemorrhage, malignant degeneration, hour-glass deformities, perigastritis, metastases, and the involvement or coincident diseases of contiguous organs.

Pyloric obstruction obtains chiefly in cases in which the ulcer is situated in the pyloric end of the stomach or in the first two inches of the duodenum. This complication is one of the easiest to diagnose. The obstruction may be partial, complete, or intermittent, as in cases of pylorospasm. Occasionally it is due to extragastric causes, chief among which are gall-bladder disease complicated by perforation, pericholecystitis involving the pylorus or duodenum by adhesions, or extensive bands constricting the outlet. In the early stages the obstruction may be temporary in character because of local swelling or edema, or it may be permanent, as the result of an old contracting ulcer. In the latter condition a compensating hypertrophy of the gastric muscle occurs, but if relief is not obtained, dilatation and atony, with varying motor insufficiency, is the natural consequence.

*Diagnosis.*—The clinical history of pyloric obstruction is usu-

\* Read before the Minn. Pathologic Society, Minneapolis, November 18, 1913. Reprinted from the American Journal of Gastro-enterology, January, 1914, pp. 111-118.

ally suggestive. The patient for a number of years has had periodic or intermittent seizures, with free intervals. As obstruction comes on the gastric disturbances are more or less continuous. Distress and pain come on sooner after meals; hypersecretion is increased, belching, bloating, and distress are more marked, and vomiting of retained food material, either spontaneously or induced, is sure to follow. The appetite is lessened, nutritional disturbances are more marked, the bowels become more constipated, and the amount of urine is diminished. In extreme types tetany, or at least incipient tetanic manifestations, is occasionally observed. On physical examination epigastric fullness is the rule, and succussion splash or peristaltic unrest may be noted. The most conclusive evidence, however, of pyloric or duodenal obstruction is afforded by the removal from the stomach of food particles or gross remnants of a meal at the expiration of six to seven hours. It is the rule in the Mayo Clinic to give a motor meal, including half-cooked rice and raw raisins (Strauss-Hansmann), twelve hours prior to the removal of the gastric contents. Following this, the distention of the stomach with air by means of an ordinary Davidson's syringe furnishes helpful data as to the outline and capacity of the organ and the detection of tenderness, spasm, and points of pain. Apparent pyloric obstruction or obvious retention may occur in cases of hour-glass deformities; the pylorospasm of an organic gastric or extragastric lesion, and rarely in advanced grades of gastropptosis with atony. In the routine fluoroscopic examination, including the radiographic plate of the stomach taken six hours after the administration of two ounces of barium sulphate in wheat-meal porridge, we have a reliable index as to the degree of stasis or obstruction.

*Incidence.*—In the 778 cases of duodenal ulcer pyloric obstruction was noted in 194, or in 26 per cent. In 324 cases of gastric ulcer obstruction was noted in 94, or 29 per cent. In 52 of 59 cases of gastric ulcer with obstruction the situation of the ulcer was classified as follows: Pyloric end, 29; lesser curvature, 20; posterior wall, two inches above pylorus, 1; pylorus and body of stomach, 1.

Perforation is the most serious and alarming of the complications. Sooner or later chronic ulcer of the stomach or duodenum involves the peritoneum. Fortunately, nature, in a large percentage of cases, has prepared for this contingency, and a protected or chronic perforation, causing adhesions and peritoneal bands, is the result. The chronic and subacute types are mainly considered in this discussion. In the latter the stomach is empty and the perforation small, or there is but a small amount of gastric contents escaping. Often a tag of omentum blocks the opening, or early adhesions form, with a small leak and a limited peritonitis or local abscess.

Pain, variable in intensity, is the rule in these cases, the degree depending directly on the acuteness of the condition. Evidence of a localized peritonitis, tenderness, muscular rigidity, and leukocytosis are present. In many of the cases of chronic perforation, however, the patient does not complain of unusually severe pain at any time during the course of the disease. Occasionally, as the result of routine examinations or unusual physical exertion, a chronic perforating ulcer becomes subacute, as evidenced at the operation. Perforating ulcers of the pyloric half or upper duodenum are limited in their course, or protected by the liver, gall-bladder, greater and lesser omenta, the colon, and the pancreas. Acute perforations, especially of the anterior gastric wall, are attended by a general peritonitis and high mortality. In the chronic and subacute cases the process of inflammation and infection is localized by the protective action of contiguous structures. Subdiaphragmatic abscess is not uncommon. One such case came under my observation two years ago, but rupture through the right diaphragm into the pleural cavity and right bronchus had already taken place. Incision and drainage through the posterior right chest resulted in a slow but complete recovery.

*Diagnosis.*—In the acute types of perforation of the duodenum the agonizing pain and prostration are suggestive, especially if an antecedent history of painful gastric disturbance has been elicited. Acute perforation, however, is frequently confused with acute appendicitis, owing to the fact that the escaping fluids, for



anatomic reasons, usually gravitate into the right iliac fossa. Thoracic disease in its incipency may simulate the pain of a perforating abdominal viscus; and a mistaken diagnosis is occasionally the cause of a needless and dangerous laparotomy. In the subacute and chronic forms the condition is more frequently confused with gall-bladder disease, especially if there be an early tendency to perforation. The diagnosis, therefore, usually depends chiefly on the symptom-complex of ulcer, associated with severe painful seizures, and upon the physical evidences of localized peritonitis or abscess. In some instances, especially when the condition is chronic and adhesions have formed, the patient complains of pulling or drawing sensations confined to the upper half of the abdomen, in raising the arms above the head, or during some similar movements. The fluoroscopic screen and radiographic plates are invaluable diagnostic agents. By these means definite evidence is usually obtainable in cases of extragastric or extraduodenal involvement, with respect to deformities or filling defects the result of contracting adhesions or other inflammatory extension. Routine radiologic examination may furnish the first conclusive evidence of a perforating ulcer of the stomach if a diverticulum can be demonstrated on the plate. Of equal diagnostic importance is the visualization of the bismuth-filled crater of a callous ulcer.

*Incidence.*—Some authorities claim, after extensive clinical and postmortem observation, that 50 per cent. of all chronic peptic ulcers eventually perforate.

In our series of 778 duodenal ulcers perforation was noted in 216 cases, or 28+ per cent. Of these, 4 were classified as acute perforating, 13 as "acute protected," 65 (8 per cent.) as subacute, and 137 (17 per cent.) as chronic perforating.

In 324 cases of gastric ulcer perforation occurred in 82, or 25.3 per cent. Twenty, or 6 per cent., were subacute, and 62, or 19 per cent., were chronic. Of the total, 78 per cent. were males and 22 per cent. were females. The average age of the males was forty-five years, and of the females, forty-two years. The duration of symptoms was extremely variable. Clinical evidence showed that in approximately 10 per cent. there was an

early tendency to perforation. It was not unusual to obtain a history of this first seizure, due to perforation, from twenty to twenty-five years prior to the time the patient sought surgical relief. In a considerable percentage of cases the continuous pain and gastric disturbance or increasingly severe attacks were most marked a few weeks to a few months prior to operation. With a few exceptions gastro-enterostomy was performed in all cases of acute perforating ulcer. In addition to the primary operation, owing to coincident disease in the gall-bladder or appendix or both, cholecystectomy was done twice, cholecystostomy 12 times, and appendectomy 37 times.

Hemorrhage in chronic ulcer of the duodenum and stomach is a less frequent complication than is generally believed. Repeated hemorrhage justifies surgical interference, although patients rarely bleed to death. A history of hemorrhage, single or repeated, in the presence of painful gastric disturbances, is the strongest presumptive evidence of the presence of an ulcer in over 90 per cent. of all cases. Hematemesis or melena, or both, has been noted in about 2 per cent. of our cases of chronic appendicitis associated with reflex gastric disturbances, and in 5 per cent. of chronic cholecystitis or cholelithiasis, or both. In the latter cases the incidence of bleeding is greater when a severe grade of infection within the gall-bladder is present, resulting in the so-called gastrototoxic hemorrhage.

The results of a recent study<sup>4</sup> by the author have shown that in 518 cases of duodenal ulcers operated on a history of hemorrhage from the mouth or bowel, or both, was present in 103, or in about 20 per cent. of cases. In 127 of these cases the ulcer had extended to and involved the pylorus. In the 94 cases of hematemesis (17 per cent.) blood has been noted in the stools in 73 (14 per cent.). In 249 cases of gastric ulcer there was hemorrhage by mouth in 54 cases (22 per cent.) and by the bowel alone in 2 (8 per cent.). In these 54 with hematemesis blood in the stools was noted 42 times. In a total of 817 gastric and duodenal ulcers an average of 23 per cent. gave evidence of gross bleeding from the stomach or bowel, or both. Smaller groups of cases, however, will give a high average

percentage of hemorrhage. Smithies, in a review of 140 cases of gastric ulcers without food retention operatively demonstrated, recorded a history of hemorrhage of variable degree in 57, or 40.7 per cent. Of this number, 47 (33.7 per cent.) had hematemesis with or without melena; 25 had hematemesis alone; 32 (22.8 per cent.) had melena, with or without hematemesis; 10 (7.1 per cent.) had melena alone; 22 (15.7 per cent.) had both hematemesis and melena.

#### MALIGNANT DEGENERATION OF GASTRIC ULCER ASSOCIATED WITH CANCER

The clinical course of a gastric ulcer tends to chronicity. An ulcer may heal either spontaneously or under favorable circumstances, combined with judicious treatment. Others tend to perforation or repeated hemorrhage. Another group may for a time pursue a chronic course, then gradually or rapidly assume all the characteristics of malignancy. In other words, a patient may for years have intermittent or continuous epigastric pain associated with gastric disturbances, which are typical of the accepted symptom-complex of chronic gastric ulcer; then within a period of six months assume all the progressive downward features, clinical, physical, and chemical, that we associate with gastric cancer. Or a circumstance which is equally striking and prognostically of as great importance are the frequent instances of apparent simple chronic ulcers, clinically and grossly, which, after microscopic examination by skilled pathologists, show early malignant hyperplastic changes in the mucosa of the borders. Invariably the subsequent course in these cases where radical operation has not been performed justifies the microscopic diagnosis. After a study of 684 specimens of ulcers and cancers, either excised or resected from the stomach, MacCarty states that the question for the clinician and surgeon is not, "Does gastric cancer develop on gastric ulcer, and what per cent. of ulcers become malignant? but has the proved association of gastric cancer with chronic gastric ulcer sufficient significance to have prognostic value in cases clinically diagnosed gastric ulcer?"

Gastric cancers may be divided clinically into two main groups: First, those with an antecedent history (average duration, eleven to twelve years) characteristic of ulcer—the cancer-following-ulcer type; definite in 41.8 per cent., and irregular in 18.7 per cent.; second, the “primary” cancers, those without an antecedent history, which may be logically interpreted as ulcer, and which constitute about 32.2 per cent. of all cancers (Smithies). In a paper before the Minnesota State Society in 1906 Graham stated his views and experiences since the late nineties relative to the etiologic relationship that exists between ulcer and cancer of the stomach. It may be conservatively stated that in all cases of gastric cancer there is clinical evidence of a preëxisting ulcer in above 55 per cent.

From 1906 to 1912 inclusive there were 691 cases of gastric cancer operated on in the Mayo Clinic. In 155 cases of this series the clinical history and gross appearance of the lesion justified the diagnosis of simple ulcer or cancer on ulcer at the operation. In this particular series a radical operation (resection and gastro-enterostomy) was performed in 97, or 62.5 per cent.; simple excision in 14; excision and gastro-enterostomy in 6; palliative gastro-enterostomy in 30, or 19 per cent.; simple exploratory in 8, and some modified operation in the remaining 4. One small group is of particular interest, and serves to illustrate a statement, previously made, namely, the association of malignant changes with chronic simple gastric ulcer. As has been noted, in 20 instances a simple excision or excision and gastro-enterostomy was performed for an apparent chronic gastric ulcer. The clinical diagnosis in each instance was ulcer, because of the typical symptom-complex; the gross appearance of the lesion *in situ* and after removal was that of simple ulcer. In these cases the average duration of symptoms was sixteen to eighteen years, the average total acidity was 52; free HCl, 43; acid salts, 13. In only one instance was achlorhydria noted. Sixteen of the patients were between the ages of forty and seventy. The lesser curvature was the site of the lesion in 12 instances, the pylorus in 3, and the posterior wall, or lesser curvature and posterior wall, in 4. The situation of the ulcer and age incidence are of peculiar significance with respect to

cancer. In all these cases there was definite microscopic evidence of cancer in the mucosa of the borders of the ulcers only.

Pathologic study tends to support the clinical evidence of the relationship between gastric ulcer and cancer. Wilson states that about 60 per cent. of malignant tumors of the stomach give pathologic evidence of preëxisting ulcer. Of these same cases there is clinical evidence on approximately 5 per cent. more. Gross and microscopic examination of smaller series may give a higher percentage. In one series 109 out of 153 undoubted cases of cancer, or 71 per cent., gave sufficient pathologic evidence of previous ulcer. In a recent review<sup>6</sup> of 684 specimens which were either excised or resected from the stomach, 191 were said to be simple chronic ulcers or ulcers in which no histologic evidence of cancer was present. "There were 472 specimens which presented the characteristics of simple ulcers plus the presence of cancer. The ulcers which contain the smallest amount of carcinomatous cells contain these in the mucosa of the borders and not in the base. Simple and multiple gastric ulcers occur which present the macroscopic characteristics of simple ulcer plus the presence of cancer in the borders and bases, indeed, with glandular involvement and metastasis."

Although duodenal ulcer of the indurated type is two or three times more common than is gastric ulcer, primary cancer of the duodenum is rare. The pathologic laboratory has specimens of 3 such cases. In 4 instances in this series cancer of the duodenum occurred by direct extension from the cancer of the pylorus. In 6 instances a primary ulcer of the duodenum extended to the pylorus, becoming malignant only on the gastric side. In about 6 cases a benign duodenal ulcer coexisted with a malignant ulcer of the stomach.

Hour-glass contraction of the stomach is of more common occurrence than was formerly believed. The contraction may occur at any point between the cardia and the pylorus, dividing the stomach into two or more portions. In our experience the greater loculus in most cases is toward the pyloric half of the stomach, due to the high situation of the ulcer on the lesser curvature or posterior wall, or both. This fact is not in agreement with

the opinion or teachings of some writers, who, conversely, state that the greater loculus is toward the cardiac end of the stomach, and that the obstruction is about 4 inches from the pylorus, as a rule. This condition is rarely congenital, and always dependent on some organic disease from one of three causes: ulcer, perigastric adhesions, or cancer. Chronic simple gastric ulcer is the etiologic factor in over 85 per cent. of hour-glass deformities. Syphilitic ulcers or cirrhosis of the stomach have undoubtedly been the underlying cause in several instances.

*Diagnosis.*—(1) Clinical. The symptoms are invariably those of chronic gastric ulcer, with or without obstruction, and in our series quite definite for ulcer in all instances. When obstruction is present, and especially if the greater loculus is toward the cardiac end, the symptoms and ordinary test-meal findings are strongly suggestive of pyloric stenosis. The presence of pathognomonic features depends largely on the site of the contraction and the degree of obstruction present between the loculi. In advanced cases, where obstruction is noted or ulceration extensive, perhaps palpable tumor and deficient acids, the evidence may be strongly suggestive of the presence of cancer. In case of mistaken diagnosis cholelithiasis has been more frequently suspected, owing to the wrong interpretation being placed on the acute pain seizure of perforation.

(2) Physical. When hour-glass contraction is suspected, careful observation at the time of gastric lavage is occasionally helpful. (a) All the water from the lavage may fail to return, some of which is apparently retained in the secondary pouch (Woelfler's first sign); (b) after a presumably thorough washing of the stomach, more contents reappear, often suggesting in appearance and odor an old retention, the washings thus being again unclean (Woelfler's second sign); or the same may be found on withdrawing the tube after washing the stomach clean and then passing it again; (c) the sign of paradoxical dilatation (Jaworski): this consists in the succussion splash on palpation, after apparent removal of all the gastric contents, a sign which is, of course, present because only the cardiac sac is emptied; (d) distention of the stomach with air

may give evidence of a tumor, first as a result of the inflation of the upper sac, then of the lower, and rarely two tumors are visible with a notch between. Patients themselves sometimes describe in their history a sensation as if the food was passing from one pouch into the other. (e) The screen and radiographic plate. This procedure gives absolute evidence of the existence of this complication. In our experience repeated instances of hour-glass deformity were noted by the fluoroscopist, in which the clinical evidence was insufficient to warrant the diagnosis, or even suggest it. The possibility of a spasmodic hour-glass, the result of ulcer or erosion, must be borne in mind. This condition usually yields to active doses of belladonna, atropin, or papaverin, and thus is differentiated from the organic or true hour-glass. Occasionally an extensive filling defect, the result of a cancerous process, may present an appearance similar to this deformity. A cancerous ulcer or tumor may itself be the cause of the hour-glass contraction. In rare instances, when hour-glass deformity was noted at operation and not diagnosed radiologically, a deep incisura of the greater curvature opposite the provocative ulcer was demonstrable on the plate. In other instances the screen and plate showed filling defects of variable extent, perhaps canalization representing the direction, extent, and degree of obstruction between the two loculi, and a bismuth-filled diverticulum indicating the situation and size of the perforating ulcer.

*Incidence.*—In 32 instances, or in 10 per cent. of the cases, hour-glass contraction had occurred. There were 19 females and 13 males. The average age in both sexes was forty-nine. The average duration of definite symptoms of ulcer was fourteen years. The shortest history was one year; the longest, thirty-nine years. Hemorrhage, usually profuse, was noted in 10, or 31 per cent.; obstruction in 9, or 27 per cent. Average total acidity, 4.7; free acids, 32; acid salts, 12 per cent. Achlorhydria was noted in 3 instances, occult blood in the gastric extract in 57 per cent. Location of the ulcer: Lesser curvature in 17; lesser curvature and posterior wall, 10; the posterior wall, 3; and the body of the stomach in 2 cases. Therefore the lesser curvature was involved

in 27 instances, or 84.4 per cent. Chronic or subacute perforation, involving the liver or pancreas, or both, obtained in 16, or 50 per cent. In 10 out of 13 cases when the posterior wall was implicated perforation was noted. In 2 cases there were 3 distinct loculi. In one case there were two distinct ulcers, both situated at the lesser curvature; there were 6 duodenal ulcers and malignant changes in 2. In 6 cases, or 0.5 per cent., hour-glass duodenum is recorded. Out of this series of 691 gastric cancers hour-glass deformity was present in 8, or 1 per cent.

*Associated Lesions.*—Routine detailed history-taking in individuals suffering from various types of abdominal pain in a large percentage of cases gives clinical evidence of probable disease or disturbance in one or more organs of the digestive tract. There is unquestionably a close interrelation, formative and physiologic, between the appendix, hepatic system, pancreas, stomach, and duodenum. Reflex epigastric disturbances, for example, in diseases of the gall-bladder and appendix, are so frequent and may so closely mimic a true gastric or duodenal lesion that in spite of careful observation and the employment of every diagnostic agent a safe conclusive diagnosis as to whether or not one or more lesions are present must often depend on the surgical exploration. Clinical and pathologic evidence is almost proof of the hypothesis that the appendix is the most frequent etiologic factor in chronic ulcerative conditions of the stomach and duodenum, and in acute and chronic infectious conditions in the gall-bladder and pancreas.

In our series of 778 duodenal ulcers the appendix showed sufficient evidence of disease, remote or more recent, to justify its removal in 193 cases, or 25 per cent. Involvement of the gall-bladder was present in 62 instances, or 8 per cent. Thus in about one-third of all duodenal ulcers there was demonstrable associated involvement of the appendix or gall-bladder, or both.

In our series of 324 gastric ulcers, 53 appendices (16 per cent.) were removed, and the gall-bladder drained or removed in 15 (4 per cent.). This makes a total of 20 per cent. of all gastric ulcers in which there was considerable disease of the appendix or gall-bladder, or both.



Pancreatitis was noted in 12 instances associated with duodenal ulcer and once with gastric ulcer. Adherence to or perforation into the body of the pancreas was common. In the duodenal ulcer group, especially when perforation had resulted, the pancreas was involved in 21 instances; in the gastric ulcer group perforation into the head or tail of the pancreas occurred in 12, and adherence to the pancreas in 13—a total of 25. Perforating ulcers of the posterior wall of the stomach naturally always involve the pancreas. In the benign lesions of the stomach there is rarely functional pancreatic disturbance.

*Incidence of Complications in Gastric Cancer.*—Of greatest clinical import is the presence or absence of metastases. The tumor may be large, yet confined to the stomach, and show no gross or histologic evidence of glandular or other involvement. Or the tumor may be small and the duration of symptoms brief, yet with evidence of metastasis into the regional lymph-nodes and even to remote organs. In all suspected cases of gastric cancer or cancerous changes in a gastric ulcer careful examination is made of the left supraclavicular area for palpable glands, of the umbilicus for malignant infiltration, the anterior rectal shelf in the male, or the tissues above and behind the uterus in the female, for evidence of pelvic metastases, and finally for free fluid in the abdomen or edema of the lower extremities. If reliable evidence of any of these conditions is present, surgical interference is useless and contraindicated.

In this series of 691 cases of gastric cancer which came to operation metastasis had already taken place in 128, or 18 per cent. None of them presented any such evidence externally. The liver was implicated in 51 cases, the pancreas in 35, mesentery and colon or both in 20, the duodenum in 7, and the pelvic organs in 13.

Pyloric obstruction was noted in 54 per cent. of all cases. Hour-glass deformity was present in 8, or 1 per cent. There was perforation to a variable degree in 24, or 3.5 per cent. In those cases in which a successful resection was performed the appendix was removed in 6 and the gall-bladder drained in 10.

## CONCLUSIONS

Pyloric obstruction or stenosis of variable degree was present in an average of 30 per cent. of all chronic simple gastric and duodenal ulcers and in 54 per cent. of all gastric cancers. This condition occurs chiefly in cases in which the ulcer is situated in or near the pylorus or in the first two inches of the duodenum. The diagnosis depends upon a history of vomiting and removal of retained food-material from the stomach; upon the demonstration, after six hours, on the Roentgen plate, of a residue of bismuth or barium sulphate administered in some suitable medium. Apparent obstruction may be due to pylorospasm. Extragastric causes are usually due to gall-bladder disease, complicated by perforation or adhesions, and implicating the pyloric end of the stomach or duodenum.

Perforation was a complicating factor in 28 per cent. of 778 cases of duodenal ulcers, in 25+ per cent. of the 324 cases of gastric ulcers, and in 3.5 per cent. of 691 cases of gastric cancer. Diagnosis is usually made on a history suggestive of ulcer, occasionally of cancer, associated with one or more attacks of acute epigastric pain. Slow chronic perforation may occur without severe pain. The diagnosis of cholelithiasis is often erroneously made in those cases in which there is an early perforation without the association of sufficient gastric disturbances suggestive or characteristic of ulcer. Perforating ulcer of the stomach is usually demonstrable on the Roentgen plate.

Hemorrhage in chronic simple ulcer of the stomach or duodenum is a less frequent complication than is generally believed. Definite profuse melena or hematemesis, or both, was noted in 20 per cent. of all duodenal and in 30 per cent. of all gastric ulcers. In a total of 817 gastric and duodenal ulcers an average of 23 per cent. gave evidence of gross bleeding from the stomach or bowel, or both. Conditions most likely to give rise to error in diagnosis are those cases of gall-bladder or appendiceal disease associated with gastric disturbances in which gastro-intestinal hemorrhage (5 per cent. and 2 per cent. respectively) of variable degree may occur.

The accepted symptom-complex of gastric ulcer is often the

precursor of gastric cancer. This association was definite in 41.8 per cent. and irregular in 18.7 per cent. of all gastric cancers in this series. Conservatively, in all cases of gastric cancer there is clinical evidence of a preëxisting ulcer in over 55 per cent. In about 60 per cent. of malignant tumors of the stomach there is pathologic evidence of preëxisting ulcer. In numerous instances when the clinical history and gross appearance of the lesion were that of benign peptic ulcer, definite microscopic evidence of malignant hyperplasia in the mucosa of the borders only was demonstrable.

Hour-glass deformity occurred in 10 per cent. of the gastric, 0.5 per cent. of all the duodenal ulcers, and 1 per cent. of the cases of gastric cancers. The diagnosis was usually made at the operating table, and was rarely made clinically until the fluoroscopic screen and Roentgen plate came into routine use.

Coincident or associated disease of the appendix (25 per cent.) or gall-bladder (8 per cent.) requiring additional operative interference was present in 33 per cent. of all the cases of duodenal ulcers; in 16 per cent. and 4 per cent. respectively, or in a total of 20 per cent. of all the cases of gastric ulcers. Pancreatitis was noted in 12 instances in the former group and once in the latter. The pancreas was usually involved when perforation was present.

The presence or absence of metastasis is of the greatest clinical import in the presence of probable gastric cancer. Even when metastasis has already taken place, external evidence is often lacking; that is, the presence of palpable glands in the left supra-clavicular space, of an infiltrated navel, free fluid in the abdomen, palpable nodules on the anterior rectal shelf in the male, or in the tissues above and behind the uterus in the female. In this series of 691 cases of gastric cancer which came to operation metastasis had already taken place in 128, or 18 per cent.

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## THE SIGNIFICANCE OF GASTRIC ULCER WITH RESPECT TO GASTRIC CANCER

### A STUDY OF 566 CONSECUTIVE OPERATIVELY AND PATHOLOGICALLY DEMONSTRATED CASES OF CANCER OF THE STOMACH\*

FRANK SMITHIES

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During the past decad there has been a growing conviction among clinical and laboratory workers that there exists an increasing number of cases clinically admitting a diagnosis only of chronic gastric ulcer which do not pursue an orthodox course of chronicity, but often rapidly assume aspects of malignant disease. If such cases come to laparotomy or necropsy, the surgeon or pathologist demonstrates cancer.

Conversely, surgically and pathologically proved cases of gastric cancer frequently reveal an early clinical history, which at any stage prior to the terminal period of evident malignancy might logically be interpreted clinically as chronic gastric ulcer.

The subject has etiologic, diagnostic and prognostic aspects. Inasmuch as this group of cases satisfies the diagnostic requirements for gastric ulcer and this process, of whatever nature it may be, later assumes characteristics that we associate with malignancy, and as we have no known medical cure for gastric neoplasms, it would appear imperative to determine how frequently this type of affection exists, in what manner, if any, it manifests itself, the possibilities of its recognition, and the indicated treatment when demonstrated. This study has been made in an endeavor to secure information in these directions.

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An analysis has been made of 566 operatively and pathologically demonstrated cases of gastric cancer from the Mayo Clinic.

#### CLINICAL CONSIDERATION

*Significance of History.*—*Sex.*—In the 566 cases there were 436 males and 130 females, or 3.1 males to each female. It will be recalled that this is almost the identical sex ratio existing in non-malignant chronic gastric ulcer.

*Age.*—The youngest patient in the series was twenty years of age; there were 26 patients aged over seventy. More than three-fourths of the cases came between the ages of forty and seventy years. A comparative study of 134 cases of non-malignant chronic gastric ulcers shows that rather more than one-half were in the forty to seventy year period.

*Etiologic Factors.*—A history of trauma was obtained in 3.4 per cent. of the cases. In 2.9 per cent. the traumatism occurred in the early history of the affection, and it was noted frequently to cause or precipitate symptoms. There were three instances in which husband and wife became affected with cancer within a few months of each other. A family or blood-relationship history was obtainable in 9.2 per cent., and a history of tuberculosis in 1.2 per cent.

*Previous Disorders of Digestion (The "Precancerous" History).*—More than ten years ago Graham called attention to the significance of the early clinical history in patients presenting themselves in his service for evident gastric cancer. He stated that more than 47 per cent. of his operatively demonstrated cases of cancer had had previous histories which strongly suggested that the cancer had followed a chronic gastric ulcer, existing variously from three to thirty-seven years. Graham also emphasized the fact that nearly 40 per cent. of his cases of cancer were not associated with the previous so-called "ulcer history," but that in this group of cases cancer developed in stomachs which previously functionated normally.

The value of early history as indicating that succeeding cancer of the stomach has its origin in such hypothetic ulcer has been

justly questioned. The weakness of the argument appears to be at least threefold: (1) The clinical variation in an ulcer symptom-complex, (2) the indefinite ideas existing as to the time element in the development of "chronic" ulcer and of cancer, and (3) the difficulties in actually proving whether or not a process which is later shown to be malignant was ever anything else. I shall consider these points seriatim.

(1) To admit the indefiniteness of an ulcer symptom-complex is to grant at once that mistakes in diagnosis are readily possible. That this is a fact has come within the experience of all gastrologists who have handled either a few or a large number of cases. In spite of personal opinions, we must admit that the only gastric ulcers that we can positively say exist are those which we can see or feel. While it may be clinically safer to treat a given case as gastric ulcer, as recommended by Shutz, nevertheless such uncertain procedures have undoubtedly led to error, confusion, and irreparable injury to patients. The prognostic aspect of the case is of greater import than the question of type of treatment based on uncertain diagnosis.

In endeavoring to gage the importance of the previous (the precancerous) gastric history of the cases in our series we found it necessary to group them according to accepted clinical symptom-complexes, of ulcer and of cancer, respectively. This mode of procedure has many faults, but it should be emphasized that this method of classification furnishes the bulk of the literature on the subject.

The clinical symptom-complex considered for gastric ulcer is based on Friedenwald's recently analyzed 409 cases, while that for cancer is compiled from the work of Osler and McCrae. If the value of such grouping is questioned, then the value of much that makes up accepted knowledge of the diagnosis and the treatment of the two ailments must also be questioned. If the symptom-complexes indicated mean clinically ulcer or cancer of the stomach, then the facts that we have to present are not without significance.

We have taken the following symptom-complex to mean gastric ulcer clinically: a form of gastric malfunction occurring usu-

ally between the ages of ten and seventy years, characterized by periodic or continuous abdominal discomfort or pain, frequently bearing definite relation to food ingestion, and often associated with epigastric or dorsal tenderness, vomiting, loss of blood (hematemesis or melena), and with hyperacid gastric contents.

We have considered as "primary" cancer, clinically, a form of gastric malfunction of a downwardly progressive nature, usually occurring in persons between the ages of forty and seventy years, who have been previously normal gastrically, the imperfect function being characterized by abdominal distress or pain, usually associated with cachexia, loss of blood, epigastric tumor, vomiting, and with gastric contents revealing motor defects, low free hydrochloric acid, and the presence of organic acids and of foreign microorganisms.

In grouping our material under these accepted clinical symptom-complexes we find that of the 566 proved cases of gastric cancer, 239, or 41.8 per cent., fall into the cancer-following-ulcer classification, while 182, or 32.1 per cent., are in the "primary" cancer division. There is, in addition, a group which may be termed cases of "irregular ulcer" that numbers 106, or 18.7 per cent. Twenty-two patients, 3.9 per cent., had a previous clinical history of gall-bladder affection, while seventeen, or 3 per cent., had early symptoms pointing to primary processes in the appendix, the pancreas, or the bowel. Combining the returns from the two ulcer groups, it is seen that precancerous history indicates that 60.5 per cent. of the subsequently demonstrated cases of cancer gave earlier clinical evidences which we associate with chronic gastric ulcer, prior to the time when the ailment assumed the clinical picture that we associate with gastric malignancy. In but 32.1 per cent. was the disease, from its inception, continuous and progressively downward, and that was in persons who had been previously sound gastrically. These figures are not to be taken as they stand to indicate that nearly two-thirds of all chronic gastric ulcers later become malignant, because we know that ulcers frequently heal spontaneously or continue as chronic, inflammatory processes. Added significance, however, is given to the figures by

the observation of the surgical pathologist that more than two-thirds of all excised chronic calloused gastric ulcers show early evidences of malignant metamorphosis (Wilson and MacCarty, and MacCarty).

(2) The analysis of any considerable material, ulcer or cancer, reveals many striking variations in the duration of the morbid process. Both clinical and pathologic differentiation should be made between the terms old and chronic as applied to ulcer and cancer. Chronicity, pathologically, does not necessarily mean that the disease is old, that is, of long duration in terms of months or years. Large, excavated, calloused ulcers may apparently develop in a few weeks, while many small, indurated round ulcers may give even obstructive symptoms for years, and this also applies to cancer. Within two weeks of the onset of disability I have seen a patient exhibit general carcinosis, with a large primary mass in the stomach. Another patient may have noticed an epigastric nodule for a year, and yet laparotomy demonstrates a small mass well confined to the wall of the stomach.

The average length of time of all symptoms in our 182 cases clinically satisfying the symptom-complex of cancer was 7.1 months. Of this group the shortest history extended over but two weeks and the longest was about three years. In nine cases (1.6 per cent.) cancer of the stomach was found at exploration, when there had been no previous indications of gastric disorder. Such cases have been described by Osler, Chesnel, and others.

Of the 239 cases clinically furnishing the symptom-complex of chronic gastric disorder previous to the period of evident malignancy, the average duration of symptoms was 11.4 years. In this group the average duration of the supervening malignant course was 6.1 months. It seems thus manifest that the periods of downward progression closely approximate in the two classes of cases, wholly independent of the earlier gastric history of the person. From our knowledge of diseased processes in general it would seem scarcely possible that the "primary" cases of cancer mentioned before existed for any considerable length of time without giving clinical evidences of their presence. Especially is this em-



phasized when we are aware that between 60 and 70 per cent. of all proved cases of gastric ulcer and gastric cancer are so located in the visceral wall as to interfere early with the stomach's emptying power. I have been frequently impressed by the fact that many so-called "primary" gastric cancers in the early weeks of their disturbance gave clinical symptoms that are commonly ascribed to chronic ulcer.

(3) The demonstration that a long-standing gastric disturbance which is later shown to be malignant was ever benign leads largely into realms of speculation. The chief arguments in support of this supposition appear to be the following: (a) After gastro-enterostomy for chronic ulcer, when the ulcer is not excised, it is stated that such a person rarely develops gastric cancer (Paterson, Gressot, and others). The argument loses much of its force when we recall that in such a patient the entire physiology of the stomach and related viscera may have been upset. It is well recognized by able surgeons and physiologists that gastro-enterostomy is more than a simple procedure of "drainage." In the large majority of gastric extracts from stomachs when gastro-enterostomy has been performed, it is possible to demonstrate, chemically or microscopically, both duodenal and jejunal contents. Just what effect these foreign substances have on gastric ulcers or gastric cancers we have yet no means of knowing. We do know, however, that the parts of the alimentary tract from which they come are rarely affected with cancer. In our series of cases of gastric cancers there are four patients who later developed cancer following gastro-enterostomy for ulcer. It also seems to hold that in cases of gastric cancer in which no pyloric obstructions are demonstrable gastro-enterostomy grants a longer lease of life than when such operations have not been performed. (b) Duodenal ulcer of the indurated type is a relatively more common affection than is gastric ulcer, yet carcinoma of the duodenum is a rarity. It is held that if cancer develops on chronic ulcer a great frequency of its duodenal incidence should be expected. That the duodenum has a protective mechanism against malignancy appears to be shown by the surgical observation that only

rarely does cancer at the pylorus, on the gastric side, pass to the duodenum by direct extension. In our series only four such instances were noted. The difference in the character of the tissue in which the chronic ulcer is implanted is also demonstrated by the fact that it is not uncommon to find that primary ulceration of the duodenum which extends up to the pylorus assumes malignant characteristics on its gastric side, while the ulcer on the duodenal side remains benign. There are six such cases in our series. We have also five cases in which malignant gastric ulcer was demonstrated together with benign calloused duodenal ulcer. Cancers of the duodenum occur, in the great majority of instances, about or below the papilla of Vater. It is well known that this region of the viscus suffers traumatism from gall-stones, altered secretion of the liver and pancreas, and from infective processes of the gall-tract. The upper part of the duodenum, where ulcer is common, is relatively immune to these influences, and also from the intense acidity and the associated peptolytic power of the gastric juice, which may irritate gastric ulcers. (c) Pathologists readily grant that there is a type of gastric affection which they class as "ulcus carcinomatosum." They demonstrate this generally at postmortem. They do not, however, demonstrate why this type of ulceration exists, by revealing any characteristic changes in the gastric mucosa in which it occurs, nor do they show that from its beginning it was ever anything but malignant. They are willing to grant that it is something different from primary cancer which later ulcerates, but just what that difference is they do not state. This type of affection appears curiously to exist as an isolated entity with no explanation of its existence or prophecy as to its future course. (d) Clinicians hold that malignant ulcer exists in from 3 to 6 per cent. of all ulcers of the stomach (Fenwick, Rosenheim). The various observers, however, do not detail just how to segregate this group clinically from chronic gastric ulcer, nor do they offer suggestions of guidance for the determination of just what chronic ulcers are destined to pursue a benign course.

In our series there were 239 cases which, up to within an average time of 6.1 months before being absolutely demonstrated as

cancer, showed nothing to indicate that were a laparotomy to be performed in that period anything other than chronic calloused gastric ulcers would be found. Only the subsequent course or the examination of fresh tissue at operation revealed the true nature of the affection. In this group of cases cancerous ulcers were found on laparotomy in 105 (43.9 per cent.), and extensive carcinomas, with or without ulceration, in 134 (56.1 per cent.). Of the 183 cases with a clinical history of primary carcinoma, *ulcus carcinomatosum* was demonstrated in 28 (15.8 per cent.), while in 154 (84.2 per cent.) extensive growth was found. Of the 106 cases with clinical history of irregular gastric ulcer in the precancerous stage, *ulcus carcinomatosum* was shown in 22 (20.7 per cent.), and in 84 (79.2 per cent.) extensive involvement, with or without secondary ulceration.

These observations suggest several points. Development and careful interpretation of the early—the precancerous—history permits patients coming to laparotomy at a stage when in more than one-half of the instances the maximum advantage of localization of the disease is available, and hence the maximum benefit accrues to the individual case. In about one-fifth of the cases of so-called primary gastric cancer *ulcus carcinomatosum* can be demonstrated at operation, and these appear to be generally favorable cases for operative procedure, compared to their fellows. This is especially to be emphasized, inasmuch as it has been shown by MacCarty and Blackford that time-duration of symptoms bears no apparent relation to the size and extent of involvement of the lymph-nodes, and that the operative and subsequent mortality are in direct proportion to the amount of involvement of the lymph-nodes.

It would appear, from the brief consideration of the objections to the interpretation of the so-called “precancerous” history with respect to the succeeding neoplasm having developed on earlier chronic gastric ulcer, as emphasized by Graham, that, so far as we can judge clinically, the careful development of such history furnishes extremely valuable diagnostic and prognostic information. It would appear from the facts submitted that such interpretation allows the greatest degree of operative benefit with the minimum

of operative risk. These facts have especially to be considered when we recall that we have no better clinical guide and that those who object to the significance of the "precancerous" history have nothing better to offer.

#### SIGNIFICANCE OF CLINICAL SYMPTOMS

*Periodicity of Symptoms.*—One of the strongest clinical evidences in the diagnosis of chronic gastric ulcer is the periodic recurrence of dyspeptic symptoms with perfect or fair health between the attacks. Graham, Friedenwald, and I have pointed this out. In 239 of the cases furnishing the material for this report in which there was a precancerous history of digestive disturbance, 81 per cent. complained of attacks of discomfort in that period, in 13.3 per cent. the attacks were of rare occurrence, and 4.7 per cent. had had continuous disturbance. When the period of malignancy supervened on the dyspeptic storm the affection was continuous and progressive in more than 99 per cent., irrespective of the earlier history. In the 182 cases making up the "primary" cancerous group, continuous disturbance was noted in 95.1 per cent. and frequent periodic attacks in 4.8 per cent.

*Types of Pain.*—In the group of cases comprising cancer following previous dyspepsia, severe pain and colics were noted in 23 per cent., steady ache in 48 per cent., and abdominal discomfort in 28 per cent. In the primary cancer group colicky pain was noted in but 6.6 per cent., steady ache in 32.4 per cent., and vague discomfort or "bloat" in 56 per cent., while in 4.3 per cent. there was no abdominal discomfort whatever. Opiate relief of pain was required in 6.5 per cent. of the first group of cases and in 2 per cent. of the second group.

*Food Relation of Abdominal Pain or Distress.*—In the diagnosis of chronic gastric ulceration, the relief of discomfort by the ingestion of food (if this form of relief be fairly constant) is granted to be a most valuable diagnostic sign. In a chronic dyspeptic its continuous presence is often almost pathogenic for ulcer. At the stage when the cases in our series came under observation, of the dyspepsia-preceding-malignancy group, food ease was present in

20.9 per cent., food aggravation in 46.4 per cent., food of negative significance in 27.4 per cent., and uncertain in 5.1 per cent. In the group of primary cancers, food ease was noted in but 3.2 per cent., food aggravation in 57.6 per cent., food of negative significance in 36.8 per cent., and of uncertain effect in 2.1 per cent.

*Hemorrhage.*—Intermittent bleeding, melena, or hematemesis, is considered as almost conclusive evidence that peptic ulcer exists. While only but from 22 to 40 per cent. (Friedenwald, Smithies) of gastric ulcers bleed, yet when hemorrhage occurs, other things being equal, it is clinically assumed that ulcer is present. In the series of cancers here analyzed, hemorrhage was noted in 97 cases. Of the group designated by history symptomatology as malignant, following ulcer, hemorrhage occurred in 62.9 per cent.; in the group styled from early history "irregular" ulcer hemorrhage occurred in 19.5 per cent., while in the group of "primary" cancers hemorrhage occurred in 16.5 per cent. Of the whole number bleeding, 52 per cent. bled at least two years prior to their coming under observation, while 42 per cent. had bled within two years of that time. In 6 per cent. the time of hemorrhage was not determined. Of those who bled within the two-year period, 77.5 per cent. comprised cases in the non-primary cancerous group.

*Anemia.*—Of one or more estimations of hemoglobin in 250 of the cases, the average hemoglobin was 69.6 per cent. for the primary cancerous group and 67.2 per cent. for the dyspepsia-before-cancer class. The average for the series was 68.1 per cent.

*Vomiting.*—Of the entire series, 326, or 57.5 per cent., of the cases vomited, and of this number 57 per cent. vomited daily. Of the series, 132 (40.5 per cent.) exhibited delayed vomiting. In but 58 (15 per cent.) was the vomitus dark or "coffee-ground."

#### SIGNIFICANCE OF PHYSICAL EXAMINATION

Tumor or ridge in the abdomen (generally epigastric) was demonstrated in 411 instances (72.6 per cent.). It was movable in 63.6 per cent. Of the primary cancerous group, tumor was present in 39.8 per cent., while in the ulcer-cancer class it was shown in 60 per cent.

Metastases were demonstrated in 86 cases (14.7 per cent.) before laparotomy, and were, in the order of frequency, rectal and pelvic, cervical and axillary, navel and abdominal wall, and in the groin. In the primary cancerous group metastases were present in 20.8 per cent., and in the non-primary class in 13 per cent. When such metastases were present, the cases were generally inoperable.

#### SIGNIFICANCE OF TEST-MEAL FINDINGS

The Ewald test-breakfast is used in the Mayo Clinic. It is preceded twelve hours by a motor meal, after the suggestions of Strauss and Hansmann. Routine quantitative and qualitative estimations are performed by the Topfer method.

There is not space here to go into elaborate detail of the information derived from examination of gastric contents in our series of 566 cases of cancer. A few of the more important points will be detailed, and the complete report reserved for a subsequent paper.

*Food Remnants.*—Motility was interfered with in 73.9 per cent. of the entire series. Of the primary cancerous group, remnants were present in 64.8 per cent. and in the non-primary group in 74.2 per cent.

*Acidity of Gastric Extract.*—In the primary cancerous group there were 55.4 per cent. of cases in which hydrochloric acid was absent, in 11.5 per cent. hydrochloric acid was between 20 and 50. In this group 79 per cent. had total acidity under 50, and 84 per cent. had combined acidity and acid salts under 50.

In the non-primary cancerous group free hydrochloric acid was absent in 49 per cent., in 20 per cent. it was between 20 and 50, and in 46.3 per cent. it was under 50. Total acidity was below 50 in 78 per cent., and combined acidity and acid salts below 50 in 90 per cent.

*Lactic Acid.*—In the primary cancerous group this was demonstrated in 52.2 per cent., while in the non-primary group it was present in 44.9 per cent.

*Occult Blood.*—This was shown (benzidin or guaiac tests) in

73 per cent. of the primary cancerous group and in 77 per cent. of the non-primary group.

*Microscopic Examinations of Gastric Extracts.*—These were made on the last 146 cases of gastric carcinoma by the agar-differential-stain method devised by the author.

*Oppler-Boas Bacilli.*—This form of organism was demonstrated in 93.8 per cent. of all the cases. In this same series yeasts were shown in 50.7 per cent. and sarcinæ in 17 per cent. Oppler-Boas bacilli and yeasts were combined in 30 per cent., Oppler-Boas bacilli and sarcinæ in 10 per cent., and Oppler-Boas bacilli together with yeasts and sarcinæ in 9.2 per cent. Cells showing atypical mitoses were present in 5 cases.

*Special Tests.*—In 141 instances of demonstrated cancer the glycytryptophan test was made. It was positive in 40 per cent.

In 31 cases the hemolytic reaction to alien erythrocytes *in vitro* was positive in 47.2 per cent.

Woodyatt and Jacques have recently pointed out that in gastric cancers an ereptic ferment, as estimated by the modified formaldehyd titration method suggested by Sorenson and Schiff, can be demonstrated in excess in the gastric extract that has been passed through a Berkefeld filter. Experience in our clinic with the original procedure is briefly summarized as follows: The average formaldehyd index of 57 cases of gastric cancer was 21; the average index of 40 cases of benign gastric ulcer was 10.8, and the average index in 75 cases of duodenal ulcer was 11.9. In 17 cases of achylia gastrica the average formaldehyd titration index was 14.1, of 10 cases of pernicious anemia, 14.5, and in 5 cases of carcinomas of the liver, 4.25. It would appear that in some instances the estimation of the ereptic power of gastric juice toward peptone solutions is of some value when taken in consideration with clinical history and symptomatology.

*Wolffe-Junghans Test for Soluble Albumin.*—By this quantitative method of estimation we have made 260 tests on gastric extracts showing achylia or free hydrochloric acid below 20 from cases in which there was no twelve-hour retention. There were 83 cases of gastric cancer in the series. The reaction was positive

in 86 per cent. In this group there were 20 cases of lesser curvature and cardiac malignancy, and the reaction was positive in 75 per cent. Of 11 cases of *ulcus carcinomatosum* without gastric retention the reaction was positive in 10 cases, or 90.9 per cent. In 11 cases of extra-gastric carcinomas (liver and gall-tract) the reaction was positive in 54 per cent. In 10 cases of pernicious anemia the reaction was positive in 10 per cent.; in 17 cases of *achylia gastrica*, positive in 17 per cent. It would seem that this test is of value when taken in consideration with other evidence in carcinomas not associated with pyloric obstruction or palpable tumor, for example, growths at the cardia, the fundus, high on the lesser curvature, and on the posterior wall, and in cases in which a large carcinoma, with considerable induration, holds a pylorus open.

We have not found either the colloidal nitrogen or antitryptic estimations of practical value.

*Roentgen Evidence.*—About 10 per cent. of ulcers and cancers are anatomically so situated as to prevent positive general clinical recognition. They are usually on the lesser curvature, high, at the cardia, fundus, and on the posterior wall. In this type of case the fluoroscope and roentgenogram often localize definitely a process and turn a clinical doubt into certainty.

#### SURGICAL CONSIDERATION

*Location.*—In 210 cases (39 per cent.) the *ulcus carcinomatosum* or the growth was at the pylorus; in 27.1 per cent. on the lesser curvature near the pylorus; in 19.3 per cent. general; in 7.2 per cent. on the posterior wall, and in 4.2 per cent. at the cardia. The greater curve was involved in 1.1 per cent., the fundus in 0.75 per cent., and the anterior wall in 0.37 per cent. In nine cases there were simple and malignant ulcers associated in the same stomach, and in five cases simple duodenal ulcer and malignant gastric ulcer.

The figures for location are to be contrasted with those of Welch, Brinton, Lebert, and others. These authorities observed generally the terminal results of cancer of the stomach, nor were their observations always in a consecutive series, examined



by uniform procedures. To any one who has had access to post-mortem material the difficulties connected with primary localization of gastric neoplasms need not be explained. The localization figures of our series, however, closely correspond to the location of chronic, calloused gastric ulcer, as shown by the tables of Welch and myself.

Lymph-nodes were involved in 71 per cent., irrespective of the early or late history. In 22.2 per cent. there was no lymph-node involvement, and these cases were, as a rule, favorable for operation. Free fluid in the abdomen was present in 3.9 per cent.; these were inoperable cases.

There were 16 cases in which a carcinomatous ulcer had been previously excised, but in which the involvement of the lymph-nodes (often microscopic only) had been noted—in which the person later returned with huge inoperable masses in the epigastrium.

Twelve per cent. of the patients died within six months following operation, but 36.6 per cent. remained well for more than three years, and 22 per cent. remained well over five years.

#### PATHOLOGY

It is not feasible to give here a detailed description of the specimens secured at laparotomy in this series of gastric cancers, and only a gross summary will be made.

The specimens were first examined in frozen section within a few minutes after their removal from the patients. They were next fixed in Melinkow's modification of Kaiserling's fluid and again sectioned and examined.

*Types of Growth.*—Adenocarcinomas were demonstrated in 556 instances (98.2 per cent.); colloid carcinomas, 5 times; fibromas, 4 times, and sarcoma once. In 155 instances (27.4 per cent.) *ulcera carcinomatosa* were shown. These may have been primarily such, had formed from previous chronic ulcer or had resulted from surface proteolytic ulceration of preceding cancer. It is often impossible to say, without clinical history or test-meal findings, whether an *ulcus carcinomatosum* developed as such or whether

it is a secondary result of a "primary" cancer. At the present stage of our knowledge the surgical pathologist can positively say only that in a given specimen of chronic, indurated gastric ulcer cancer is or is not present. There appears to be a borderline class, however, in which surgical pathologists of the widest experience in the examination of fresh tissue can often distinguish cellular arrangement or intracellular change of such nature as to warrant their stating that the process is "precancerous." Not infrequently the subsequent course of the ailment bears out the histologic prophecy.

In the experience of Wilson and MacCarty, 71 per cent. of 153 cases of undoubted gastric carcinomas presented gross and microscopic evidence of previous ulcer. These observers also demonstrated that 68 per cent. of resected chronic ulcers of the stomach and duodenum (the latter furnishing a very small proportion of cases) were associated with cancer. In several instances MacCarty noted that the presence of erosions, simple round ulcer, and *ulcus carcinomatosum* in the same specimen suggested possibilities of transition corresponding to that shown by Woolley in cases of adrenal tumor. MacCarty has emphasized the difficulties of always differentiating between simple hyperplasia and malignant hyperplasia. He suggests that hyperplasia is a forerunner of malignancy, that hyperplasia varies in degree, that cancer is malignant hyperplasia, which also varies in degree, and that some degree of both processes are indistinguishable, histologically. This view is well within the opinion of Adami. It seems to be partially substantiated by the recent work of Drew and Levin in experimental tissue proliferation and inoculation of malignant tumors.

*Association of Malignant and Benign Processes.*—In this series of gastric cancers there were 5 instances of simple ulcer of the duodenum associated with malignant gastric ulcer. In 9 cases simple and malignant ulcers were found in the same stomach. Independent cancer of the stomach and of the duodenum was demonstrated once. There were 2 cases of multiple gastric cancers. Six times it was observed that malignant gastric ulcers stopped

sharply when duodenal mucosa was reached, but in 7 instances of extensive gastric cancers it was shown that the duodenum was secondarily involved by direct extension.

#### SUMMARY

1. A number of cases clinically admitting only a diagnosis of chronic gastric ulcer are shown to be malignant at operation. Many cases of gastric cancer reveal a "precancerous" history, which at any stage prior to the terminal period of malignancy satisfies the clinical symptom-complex of chronic gastric ulcer.

2. A study of 566 consecutive cases of gastric cancer, operatively and pathologically demonstrated, has been made in the attempt to determine how frequently chronic ulcer precedes gastric cancer and how this change is manifested clinically.

*Clinical Consideration.*—The sex ratio in gastric cancer is approximately that of chronic gastric ulcer (3.1 males to 1 female). More than three-fourths of the cases of gastric cancer occur in persons between the ages of forty and seventy years; more than one-half those of chronic gastric ulcer (134 cases) between the ages of forty and seventy. A family history or one of blood-relationship of gastric cancer existed in 9.2 per cent.—a history of tuberculosis in 1.2 per cent.

Precancerous history indicates that 41.8 per cent. of proved cases of gastric cancer presented early symptomatology of chronic gastric ulcer; 18.7 per cent. showed the early symptomatology of "irregular" gastric ulcer, and 32.1 per cent. of the cases had the symptom-complex of gastric cancer, without previous gastric malfunction. Thus in more than 60 per cent. of the cases of gastric cancer the patients had previous dyspeptic history and this history was generally that of chronic gastric ulcer.

The length of time of all symptoms of the "primary" cancerous group (182 cases) was 7.1 months. The average length of time of the precancerous dyspeptic period in 239 cases was 11.4 years. In this group the supervening period of evident malignancy averaged 6.1 months.

Development of precancerous history permits patients coming

to laparotomy at a stage when in more than one-half of the instances surgical advantages of a localized process are available. In about one-fifth of the cases of "primary" gastric cancers, ulcer carcinomatosum is demonstrated operatively.

*Significance of Clinical Symptoms.*—Periodicity: In 81 per cent. of the cases in which prolonged dyspepsia had preceded cancer periodicity of symptoms was noted in that stage, while in 99 per cent. of the cases periodicity was absent when the process became evidently malignant. In but 4.8 per cent. of 182 cases of "primary" cancer were there periodic attacks of distress.

*Types of Pain.*—Nearly one-fourth of the patients in whom dyspepsia preceded malignancy had prostrating pain (colics, etc.), while only about one-fifteenth of the patients with "primary" cancer exhibited this type of distress. Opiate relief was required in 6.5 per cent. of the former class and in 2 per cent. of the latter.

Food ease of pain was present in more than one-fifth of the cases in which malignancy followed clinical chronic gastric ulcer and in 3.2 per cent. of the "primary" cancer group.

*Hemorrhage.*—Melena or hematemesis was noted in 17.1 per cent. of the cases. Of the group styled malignancy following ulcer, hemorrhage occurred in 62.9 per cent.; in the "irregular ulcer" group before malignancy, in 19.5 per cent., and in "primary" cancer group, 16.5 per cent. Of patients bleeding within two years of coming under observation, more than three-fourths fell in the ulcer-before-cancer classification.

Hemoglobin estimation was rather higher in the primary cancer group than the ulcer-preceding-malignancy class.

Vomiting was observed in more than 57 per cent. of the cases of gastric cancer. More than 40 per cent. exhibited delayed vomiting. Of the entire group, 15 per cent. gave a history of dark or "coffee-ground" vomit.

Nearly three-fourths of the cases of gastric cancer exhibit abdominal tumor or ridge. This is present in nearly two-fifths of the cases of "primary" cancer and more than three-fifths of the cases in which ulcer preceded malignancy clinically.

In more than one-fifth of the cases in the "primary" cancer

division and in about one-ninth of the cases in the non-primary group, metastases were demonstrated before laparotomy.

*Test-meal Findings.*—Delayed gastric emptying power was evidenced in nearly two-thirds of the cases in the primary cancer class and in nearly three-fourths of cases in the non-primary division.

*Acidity.*—In 55.4 per cent. of primary gastric cancer cases free hydrochloric acid was absent; in 11.5 per cent. it was between 20 and 50.

In the non-primary cancer class free hydrochloric acid was absent in 49 per cent., and in 20 per cent. it was between 20 and 50.

*Lactic Acid.*—This is more commonly noted in the primary cancer group than in the non-primary division.

*Occult Blood.*—This is rather more frequently demonstrated in the non-primary cancer class than in the primary cancer group.

*Oppler-Boas Bacilli.*—These were demonstrated in 93.8 per cent. of cases of gastric cancer by the differential agar-stain method.

*Glycyltryptophan Test.*—This was positive in 40 per cent. of the cases (141). The *hemolytic* reaction was positive in 47.2 per cent. of the cases (31). The *formaldehyd titration index* was uniformly higher in gastric cancer and ulcera carcinomatosa than in other gastric ailments. The estimation of soluble albumin by the *Wolff-Junghans test* was more uniformly positive in cancer and carcinomatous ulcer cases than other forms of gastric disturbance.

*Roentgen-Ray Evidence.*—In about 10 per cent. of the cases of gastric cancer evidence returned by fluoroscope and roentgenogram is of distinct value in making absolute diagnosis of physically inaccessible located cancers.

*Surgical Consideration.*—The locations of ulcera carcinomatosa and cancer as shown by laparotomy closely approximate those of chronic gastric ulcer, but do not correspond to the postmortem localization of gastric cancer. More than one-fifth of the cases of gastric cancer revealed no involvement of the lymph-nodes, with generally favorable operative outlook. In nearly 4 per cent. free abdominal fluid was present. These were inoperable cases.

*Pathology.*—More than 98 per cent. of gastric cancers were

adenocarcinomas. Sarcoma occurred but once in 566 cases. More than one-fourth of gastric cancers show ulcerative changes, as primary or secondary type of growth. It is usually an easy matter to state definitely whether or not a given specimen is at the time benign or malignant. There is a group of cases of chronic ulcer in which examination of fresh tissue reveals cellular or intracellular variations of such type as to warrant designation of "pre-cancerous" ulcer. It is often impossible to distinguish stages of simple and malignant hyperplasia histologically. Benign ulcers of the duodenum may be associated with malignant gastric ulcers. Benign and malignant ulcers may be associated in the same stomach.

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# THE TECHNIC OF ROENTGEN EXAMINATION OF THE GASTRO-INTESTINAL TRACT, AND THE INTERPRETATION OF SCREEN AND PLATE FINDINGS \*

R. D. CARMAN

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The fundamental principle of Roentgen-ray examinations of the stomach and intestine is the visualization of their outline by filling them with substances opaque to the ray, a principle which we owe to Rieder, of Munich, who, in 1904, first used bismuth subnitrate for the purpose. From this has evolved the present-day technic of radiography of the digestive tract, the evolution being contributed to in minor particulars by numerous roentgenologists, and in major particulars by a few men, of whom Holzkecht and Haudek stand out with signal prominence.

The occasional toxicity of bismuth subnitrate soon led to its supersession by bismuth subcarbonate and later the oxychlorid. Zirconium oxid has also been employed to some extent abroad. Chemically pure barium sulphate, because of its cheapness, has come into very general use both for enemas and for the opaque meal.

Bismuth subcarbonate is in common use. By its alkalinity peristaltic activity is depressed somewhat. The oxychlorid being lighter, is consequently better held in suspension. It does not interfere with peristalsis.

The finding of a suitable medium for the administration of the opaque salts by ingestion at the time of examination has given

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some difficulty. It is desirable that the mixture be more or less palatable, that it be thick enough to hold the opaque salt in good suspension, yet not too thick to fill all recesses, that it be not too stimulative of gastric secretion, and that it do not suppress peristalsis or produce early pyloric closure. When a large number of cases are examined the cost becomes a matter of importance.

The vehicles commonly used include water, milk (plain, condensed, or fermented), mucilage of acacia, potato-starch, and various cereals. Each of these has its advantages and disadvantages, depending on the purpose in view. For the six-hour Haudek meal a cereal, such as one of the wheat breakfast foods, with a little sugar and cream or fruit syrup, is desirable. At the beginning of the screen examination a little plain water and bismuth facilitates palpatory outlining of the borders of the stomach, and by not exciting the pyloric reflex can ordinarily be expressed into the cap and duodenum, thus visualizing them. For complete filling of the stomach, preparatory to radiography, the bottled proprietary fermented milks are admirable. They are relished by most patients, hold the bismuth in good suspension, and do not hinder peristaltic action. Mucilage of acacia, freshly made from the powder or gum, is effective, but not pleasant to take. The semi-condensed milk holds up to the bismuth fairly well and is palatable. Owing to its contained fat, peristalsis is much diminished. Two ounces of potato-starch in 6 or 8 pints of water, well stirred and brought to the boiling-point (after the Gourevitsch formula), makes an excellent medium. It can be flavored with fruit syrup to suit the taste.

The essentials of an opaque enema are: (1) that the mixture shall not be irritating to the bowel; (2) that it shall be sufficiently large to fill the entire colon; (3) that it shall be sufficiently fluid to flow freely and fill recesses, yet thick enough to hold the bismuth in good suspension.

Barium sulphate, bismuth subcarbonate, and bismuth oxychlorid are each commonly used as a base. Barium sulphate serves the purpose well and is far cheaper than bismuth. Bolus alba (kaolin) is added by some.



For media, mucilage of acacia, fermented milk, condensed milk, mucilage of tragacanth, potato-starch, and other vehicles are employed. Any one of them can be used satisfactorily. The potato-starch is more economic, but has the occasional disadvantage of becoming lumpy and obstructing the enema tube unless filtered.

The medium should be from 50 to 60 ounces in amount, should contain from 4 to 6 ounces of bismuth (subcarbonate or oxychlorid)

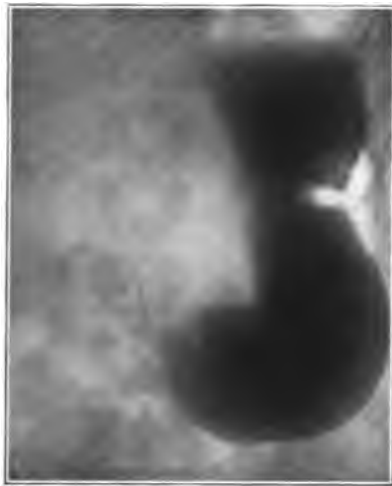


Fig. 13.—(A80,973, X-ray 19,835.) W. E. W., female, aged forty-four. Radiogram shows a "fish-hook" stomach. There was no residue after six hours. It shows a projection on the lesser curvature, which is the bismuth-filled crater of a callous ulcer, and a marked transverse contraction of the greater curvature (incisura) opposite this niche. Diagnosis: Callous ulcer on lesser curvature. Operation: Excision of ulcer on lesser curvature, about 5 inches from pylorus, with surrounding fibrous tissue; gastroduodenostomy. Pathologic report: Gastric ulcer, scar tissue. (Clinically, this patient's symptoms were quite insufficient to establish the diagnosis and she was about to be sent home when an x-ray examination was made.)

or from 6 to 8 ounces of barium sulphate, thoroughly mixed, should be warmed to or slightly above the body temperature, and should be administered by gravity-pressure from a height of from 3 to 6 feet. The ordinary hard-rubber saline tip is sufficient, the so-called high enema being unnecessary. The rubber tubing should be equipped with a spring-clip cut-off.

After completion of the examination the patient should evacuate the enema at once. I have not found purgatives necessary

afterward, nor has caking of the bismuth or barium in the bowel, as mentioned by some radiologists, occurred to my knowledge.

In those cases in which the opaque enema meets with complete obstruction at any point, it may be supplemented by an opaque meal. By watching the progress of the latter the proximal limit of the obstruction can thus be determined.

Proper preparation of the patient for examination is important. In order that the bismuth may fill and outline the stomach and bowel it is obviously necessary that they be evacuated beforehand as completely as possible. In most cases this can be effected by the administration of a saline or castor oil the evening previous to the examination, and, if an opaque enema is to be given, the patient should also wash out the bowel with a soap-suds injection early on the morning of examination. Even with these precautions there will be more or less annoyance to the examiner from gas in the bowel, and the roentgenologist who can devise a technic which will entirely eliminate this annoyance will indeed be fortunate. The patient should abstain from food from the evening previous to examination until after its completion.

A uniform technic in regard to opaque ingesta and injecta will give a stable basis of comparison and greater uniformity of results.

#### PROTECTION

Fluoroscopy, being so advantageous in gastro-intestinal work, attention is directed anew to its possible dangers. With the disasters which have befallen pioneers in Roentgen-ray work fresh in our minds, we have an acute, perhaps exaggerated sense of the hazard attending such work, especially screen work. I would not urge any roentgenologist to take risks which to him seem imprudent and which might possibly result in his injury, but candor compels me to express my very sincere belief that we have gone from one extreme to the other, from extraordinary and ignorant rashness to extraordinary and unnecessary caution. This excessive caution is shown in much of the modern screen apparatus. In the effort to secure protection many of the installations have been made complicated, unwieldy, and often inefficient. Access

to the patient for close inspection and palpation has been rendered difficult or even impossible, and the screen examination thus "denatured" loses half its interest and value. In a personal communication Haudek states that with quite simple apparatus he has screened over 12,000 patients without harm to himself or to them.

The apparatus which I have used for several years, making hundreds of screen examinations in that period, without the



Fig. 14.—(A83,115, X-ray 20,799.) A. C., female, aged sixty-two. Radiogram shows "fish hook" stomach with a moderately large projection on the lesser curvature which was regarded as perforating ulcer. No transverse contraction seen. Small residue after six hours. Operation: Resection one-half middle of stomach; end-to-end union. Pathologic report: Carcinomatous ulcer with glandular involvement.

slightest injury to the patients or myself of which I am aware, is not at all complicated. The tube is encased in a box thickly painted with lead oxid, mounted on a shaft, which is given free vertical and lateral movement by means of counterweights within the upright standards at each end of the shaft. The opening in the tube-box has a rectangular diaphragm. Immediately in front of this is a shield of sheet lead  $\frac{1}{8}$  inch thick, 7 feet high and 5 feet wide. A central panel of this shield is cut away and replaced by a thin sheet of aluminum against which the patient leans. The

screen hangs in front of the patient from an arm attached to the tube-box, with which it moves in unison. I usually wear a leaded rubber apron and gloves. A portable switch-table stands conveniently at the left, and a foot-switch on the floor.

After the screen examination plates are made with the patient in a standing posture, an adjustable tube-stand being used, and the cassette fixed on a movable wooden bracket attached to the wall.

For examinations of the colon we use a lead-lined wooden table, open on the side away from the operator. Beneath this the tube, mounted on an arm, swings freely in every direction in unison with the screen attached to another arm above the table. At the foot of the table is an upright with pulley and cord for adjusting the enema-container at various heights. The top of the table is of canvas, on which the patient lies. The tube has an iris diaphragm.

Before beginning a screen examination the observer will find it advantageous to remain in the dark-room for from ten to twenty minutes in order to give his eyes a maximum of accommodation. He will thus be enabled to see details on the screen which would otherwise be invisible. A pair of closely fitting, smoked-glass goggles, to be worn whenever it is necessary to turn on the room lights, will help to maintain the accommodation and lessen eye-strain.

#### A ROUTINE EXAMINATION OF THE STOMACH

Having taken an ounce of castor oil the evening before, the patient reports in the morning without breakfast. He is then given an ordinary portion of wheat-meal porridge into which two ounces of barium sulphate has been well mixed, together with a little sugar and cream. He is directed to abstain from further food until after the examination, and to return six hours later. On his return he is stripped down to the hips; the screen is placed against the abdomen, and the presence or absence of residue in the stomach from the morning meal noted.

Next the "head" of the barium column, that is to say, the most advanced position in the intestine of the six-hour meal, is determined. Commonly this will be in the cecum, but it may be

anywhere from the stomach to the rectum, depending on the patency and motility of the tract.

The patient now drinks rapidly 6 or 8 ounces of water containing  $1\frac{1}{2}$  to 2 ounces of bismuth subcarbonate, well stirred. Its entrance and descent into the stomach are carefully watched. When all has been drunk, the observer palpates toward the pylorus and by this effleurage is often able to drive a quantity through into the duodenum, thus visualizing it. He then presses the bis-



Fig. 15.—(A80,993, X-ray 19,816.) J. K., female, aged thirty-seven. Radiogram shows cap and duodenum visualized throughout, with lagging of bismuth. No residue after six hours. This picture is frequently seen in duodenal ulcer and illustrates the necessity of correlating the x-ray with the clinical findings. Operation: Cholecystectomy for typical strawberry gall-bladder with a diverticulum.

muth in the stomach upward, watching the outline of the greater and lesser curvatures.

Sixteen ounces of potato-starch pap containing 2 ounces of bismuth subcarbonate and flavored with syrup of raspberry are then drunk by the patient. Usually this fills the stomach quite well, outlining it clearly. Irregularities which may have been previously observed with the bismuth water are palpated to de-

termine their nature and permanence. Mobility and peristalsis are also determined.

Two or three plates are now made, the patient standing with his abdomen against the plate-holder, with the upper edge of the plate at or near the nipples.

#### A ROUTINE EXAMINATION OF THE COLON

Having taken an ounce of castor oil the evening before, and a cleansing soap-suds enema the morning of examination, the patient strips and lies on his back on the colon-table. The enema, 16 ounces of mucilage of acacia and 3 cans of condensed milk with 8 ounces of barium sulphate, is warmed to body temperature, put into the container, and elevated from 3 to 6 feet above the table. The syringe-tip is introduced into the rectum and the flow released by the spring-clip. On the screen the enema is seen slowly to fill the ampulla, then successively the sigmoid, descending, transverse, and ascending colons and the cecum, occasionally passing the ileocecal valve into the ileum, and, more rarely, filling the appendix.

The abdomen is palpated at intervals to determine the mobility and elucidate eccentric loops and apparent kinks of the bowel. If definite obstruction, not disappearing on massage, is met with, or if the patient complains greatly of discomfort, administration of the enema is stopped.

The plates (14 by 17) are made with the patient standing or reclining, or both.

#### DIAGNOSTICS OF THE SCREEN-EXAMINATION OF THE STOMACH

*Motility.*—Mere traces being excluded as unimportant, a distinct residue from the Rieder meal after six hours, no additional food having been taken meanwhile, is a valuable diagnostic indication. A small residue, up to a quarter of the meal, may be found in atony and hyperacidity, but organic disease must not be overlooked. A large residue of half or more of the meal often signifies obstruction either at the pylorus or in the duodenum. It may occur in carcinoma involving the pyloric end of the stomach, in

pyloric and duodenal ulcer with contraction or adhesions, and in adhesions about the gall-bladder, stenosing the duodenum or pylorus. A residue associated with hyperacidity is sometimes found in gastric ulcer.

In carcinoma not obstructing the pylorus clearance is early. Here there is commonly the accelerating factor of achylia, and not infrequently the pylorus is gaping, as though stiffened by infiltration. The head of the bismuth column in the intestine, usually in the cecum or ascending colon after six hours, may be advanced by



Fig. 16.—(A74,843, X-ray 17,585.) O. H. L., male, aged fifty-seven. Radiogram shows marked filling defect of the pars cardiaca and media. Possible carcinoma of stomach. Operation: Carcinoma cardiac end of stomach. Extensive glandular involvement. Also metastasis in pelvis.

low gastric acidity to the transverse colon, the splenic flexure, or even beyond, while with gastric hyperacidity the head is often in the ileum. The position of the head is therefore a gross measure of acidity if no mechanical obstruction exists. If barium be used in the Rieder meal, the head will usually be found farther advanced than if bismuth is used. After six hours the barium will quite commonly be found in the transverse colon.

*Form.*—It has been remarked that the stomachs of different individuals as seen by the Roentgen-ray vary in shape as much as their faces do. Nevertheless, the vast majority fall into two gen-

eral classes—the “fishhook” and the “steer-horn.” Each of these has its variations, to some of which distinctive names have been applied. The “fish-hook” form, the “J” shape, is that most commonly met with and seen. It occurs in nearly all women and in many men. The “habitus enteroptoticus” of Stiller, characterized by a long, narrow trunk and a narrow costal arch, is usually accompanied by a “fish-hook” stomach. Ulcer is found more often in the “fish-hook” than in the other type. The “steer-horn” (or cow-horn) stomach is aptly described by its name. It occurs rather frequently in men and occasionally in women, its possessor nearly always having a short, broad trunk and a wide costal arch. The “steer-horn” type is more often associated with carcinoma than the other type.

Hour-glass stomach is the name applied to a striking and important deformity of the organ. Sometimes this is produced by spasm of a bundle of circular fibers, not quite completely dividing the stomach into two chambers, both of which are rather symmetric, with regular outlines. The spasmodic hour-glass can often be made to disappear by vigorous palpation, the patient being asked to breathe with open mouth and his attention being thus distracted. In long, ptosed stomachs the first swallows of bis-muth are sometimes held up momentarily in the funnel-shaped cardia, then drop through into the more expanded lower segment. This condition should not be confounded with hour-glass stomach.

Organic hour-glass stomach may be produced by adhesions or the scar contraction of ulcer, or by the deforming effect of carcinoma. The segments (loculi) are usually unequal in size, asymmetric, and irregular in outline. In carcinoma the canal between the segments is usually longer than in ulcer and more or less central between the curvatures; it is short in ulcer, as a rule, and nearer to the lesser curvature. Hour-glass stomach may be overlooked if filling of the lower segment is greatly retarded.

*Diverticulum.*—Hour-glass deformity frequently, but not always, accompanies perforating ulcer with diverticulum. The perforation may be anteriorly into the liver, or posteriorly into the pancreas, and the cavity formed by the continuation of the ulcera-



tive process in these organs is the diverticulum. It shows on the screen as a sort of miniature stomach, of varying size, just outside the outline of the stomach, usually on the lesser curvature, but may also be seen on the anterior or posterior wall, with a layer of

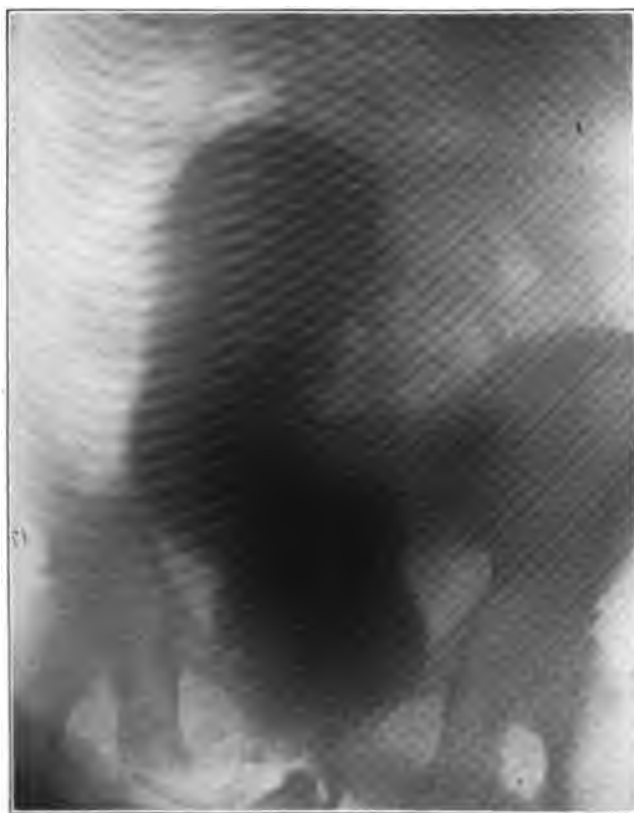


Fig. 17.—(A80,028, X-ray 19,406.) R. B. B., male, aged thirty-seven. Radiogram shows obstruction of descending colon and sigmoid, probably due to tumor. Exploration: Tumor of sigmoid 7 inches long fixed to the bladder and left side of pelvis. Inoperable carcinoma.

bismuth and a layer of less dense fluid, surmounted by a gas-bubble. Whether the diverticulum be in the liver or the pancreas may sometimes be determined by rotating the patient, the horizontal arc of movement being greater in the latter instance. Di-

verticulum in the liver, being closer to the screen, is sharper in outline than diverticulum in the pancreas and shows respiratory excursion. A bismuth residue will often remain in the diverticulum after the stomach is empty.

*Position.*—With the patient standing, the position of the stomach depends somewhat on its form. A “steer-horn” stomach passes obliquely downward across the spine, while the cardia and media of a “fish-hook” stomach usually hang vertically, the pyloric end crossing the spine and curving upward. Between these are numerous normal variations. The lower border of the average bismuth-filled stomach is at or near the umbilicus, but the type must be taken into consideration, the “steer-horn” being often above, and the “fish-hook” at or below. An inch above and an inch to the right of the umbilicus is an average position of the pylorus. This corresponds nearly to the second lumbar vertebra. The point has been made that, as the cardiac end of the stomach is fixed, genuine gastropnoptosis seldom exists. Elongation of the stomach with the lower pole down even to the pubic arch is not uncommon, especially in women.

The pylorus may be displaced to the left by the contraction of an ulcer-scar on the lesser curvature, upward and to the right by periduodenal and pericyclic contractions, and downward in association with splanchnoptosis. In pyloric stenosis it is frequently seen displaced to the right.

*Tonus.*—This is the degree of ability of the stomach so to contract on its contents as to maintain a tubular form until empty. Degrees of tonicity are designated as hypertonic, orthotonic, hypotonic, and atonic.

The hypertonic stomach supports its contents with a firm grasp. Either type may be hypertonic: the “steer-horn” is almost constantly so. The orthotonic represents the normal or average tone, while the hypotonic is undertone, usually having a broader lower pole, and is seen more often in the “fish-hook” type. The atonic stomach, completely without tone, unable to hold up its contents in columnar form, hangs as a flaccid bag, with its vertical walls usually in apposition. It is seen typically in pyloric

obstruction with the lower pole expanded into a wide basin and the vertical segment of the stomach unfilled.

*Gas-bubble*.—At the upper end of the cardia is a clear, dome-like area, its base on a level with the esophageal opening. This

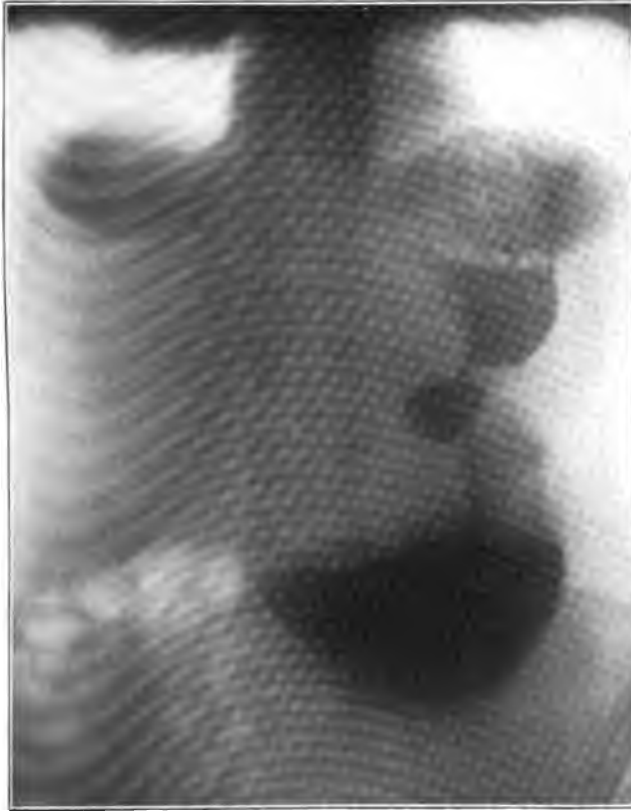


Fig. 18.—(A77,398, X-ray 18,393.) J. S. M., female, aged fifty-four. Hour-glass stomach, "fish-hook" type, displaced to the left, extending below umbilicus, showing diverticulum just outside stomach outline on lesser curvature. Diverticulum contained bismuth after the upper loculus had emptied. Diagnosis: Diverticulum due to perforating ulcer of the stomach. Operation: Perforating gastric ulcer of stomach, perforating into the liver.

is the gas-bubble (*Magenblase*). Its size varies considerably. In aërophagy, in carcinoma, and in neurotics it may be quite large. In unfilled, ptosed stomachs its shape may be fusiform and its size quite large.

*Mobility.*—Except its cardiac end, the normal stomach can be moved about quite freely. Fixation, or restricted mobility, is therefore of significance. Adhesions from penetrating gastric ulcer or new-growths may be the cause. At the pyloric end an inflammatory process about the gall-bladder or about an ulcer of the duodenum may lessen the normal range of movement.

*Peristalsis.*—A normal peristaltic wave appears as a shallow indentation on the greater curvature, at or near the incisura cardiaca (an indentation marking the juncture of the cardia and media), and travels slowly toward the antrum, growing deeper as it progresses. On the lesser curvature the wave travels a much shorter distance to the incisura angularis (a depression at the beginning of the antrum), is deeper than its fellow on the greater curvature, and apparently slightly in advance of it. The antrum seems to efface itself by concentric contraction, and is immediately succeeded by another, the formation of which is in progress while the old antrum is disappearing.

Average peristaltic waves occur at intervals of from ten to twenty seconds. Sometimes three or four may be seen simultaneously. Peristaltic activity is increased by high acidity. It can be stimulated by palpatory manipulation, but quickly subsides. In atonic, dilated stomachs the number and depth of the waves are greatly diminished. In pyloric and duodenal obstruction of recent existence the waves may be tremendously exaggerated, almost bisecting the stomach. In carcinoma a wave will progress to an infiltrated area, skip it, and take up its course again in the unaffected wall beyond.

The character of the opaque ingesta employed often materially influences peristaltic action as to force and frequency.

*Antiperistalsis.*—This, as observed first by Jonas, is described as a less active, wave-like movement in the reverse direction, sometimes coexistent with normal peristalsis, seen occasionally in pyloric obstruction and in other organic lesions of the stomach. In many hundred examinations of the stomach I have never seen this phenomenon.

*Secretion.*—Below the gas-bubble, at the top of the bismuth

column, may be seen a defined layer of fluid less opaque than the bismuth pap. The depth of this layer is regarded by some as an index of the stomach's secretory activity. When the bismuth is given in solid media, this opinion is, no doubt, well founded, but

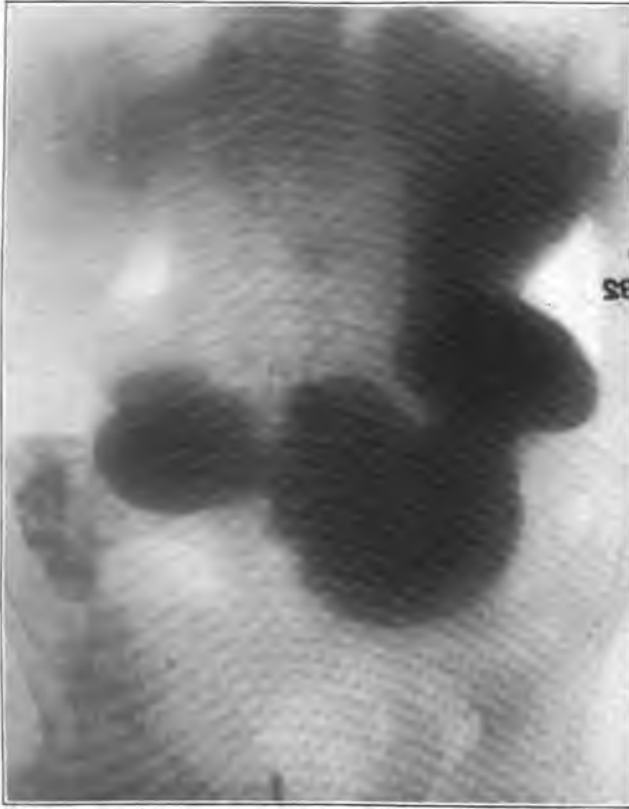


Fig. 19.—(A79,785, X-ray 19,282.) D. A. C., male, aged fifty-two. Screen showed a large six-hour residue. Tremendous peristalsis showing 3 cycles. Diagnosis: Pyloric obstruction. Operation: Large duodenal ulcer, size of a penny. Very marked obstruction, lumen reduced to size of a lead-pencil. Operation, Heineke-Mikulicz type, without pyloroplasty.

if watery media are used, out of which water may separate, the result is open to question.

Kaestle's capsules are sometimes used to determine the amount of secretion in an otherwise empty stomach. They are given in

pairs, a "sinking" and a "swimming" capsule, each containing enough bismuth to be visualized by the Roentgen-ray. The vertical distance between the "sinking" capsule at the bottom and the "swimming" capsule on the surface of the secretion shows its depth. Objection may be made, however, that the amount of secretion would also depend on the extent of its surface, which in turn would be governed by the broad or narrow curvature of the lower pole. After swallowing the capsules the patient may be allowed to chew appetizing morsels of food, but not swallow them, thus stimulating secretion. Secretion is far more accurately determinable by the gastrologist, however, than by the radiographer.

*Pylorus*.—Immediately after giving the bismuth-water this can usually be expressed by the effleurage into the first portion of the duodenum—the cap. The pylorus will then be shown as a clear disk, from an eighth to a quarter of an inch thick, seen edge-wise, with a central narrow column of bismuth joining that in the cap and the antrum.

Pylorospasm from hyperacidity or from numerous reflex causes, such as lesions of the gall-bladder, chronic appendicitis, nervousness, fright, etc., may make it difficult or impossible to press the contents of the stomach beyond the pylorus and thus localize it. Duodenal ulcer is frequently associated with a freely patent pylorus, evidenced by the ease with which the bismuth passes through it or can be pressed through it. I have found that pressure over the right iliac fossa will often be followed by upward retraction of the stomach and free flow of its contents into the duodenum.

*Filling Defects*.—A filling defect is an irregularity of outline caused by the encroachment of an intrinsic tumor on the lumen of the stomach. In medullary carcinoma the visualized periphery of the lumen, instead of its normally smooth outline, may show a gnawed, ragged, notched, irregular appearance, sometimes corresponding to a palpable tumor-mass at that point. Either curvature or both may be involved. The "steer-horn" stomach with an infiltrating scirrhus carcinoma may be narrowed to an eccentric-looking curved funnel, defective filling being evident, though the walls are only slightly uneven.

A true filling defect must be determined by palpation after the water-bismuth has been taken, and again after the pap. It must be differentiated from the irregularity produced by an adjacent



Fig. 20.—(A80,853, X-ray, 19,797.) J. O. S., male, aged thirty-two. Marked redundancy of sigmoid with loop folded on itself. Marked obstruction transverse colon near splenic flexure, no bismuth going beyond point of obstruction. Remainder of transverse, ascending colon and cecum contain a small amount of colonic gas. Diagnosis: Probable tumor of transverse colon. Operation: Carcinoma of transverse colon.

gas-filled colon, such as is noted frequently at the splenic flexure. Alterations of the contour of the stomach by adjacent extrinsic tumors are not easily distinguished from those due to intrinsic

lesions. Filling defects may be produced by gummas of the wall of the stomach. These cannot always be differentiated radiologically from carcinoma. Even though fairly regular in outline, an extraordinarily small stomach, especially if short, is open to suspicion.

*Incisura.*—In the outline of the stomach, especially on the greater curvature of the pars media, there is sometimes seen an abnormal indentation of varying width and depth, with its upper and lower borders commonly parallel, its apex rather more blunt than that of a peristaltic wave, and not moving toward the pylorus. This transverse contraction is the incisura, first pointed out by Reiche as an index of gastric ulcer. Its production is believed to be due to the irritation from the ulcer or its scar, causing spastic contraction of the circular muscle-fibers at that point.

An incisura may occur transitorily, disappearing of itself or after palpatory manipulation. Eisler has seen these transitory incisura in small ulcers and erosions. Some roentgenologists question the significance of the fleeting phenomenon and believe that it may result as a reflex or functional disturbance. Leaving this aside, however, a typical incisura, showing more or less persistence, not disappearing on manipulation, and found at repeated examinations, is generally accepted as diagnostic of ulcer, especially if it corresponds to a pressure-pain point on the lesser curvature. At this latter point there may sometimes be seen a bud-like projection—the bismuth-filled crater of an ulcer.

Double incisura have been found associated with double ulcer. However, I have not seen this phenomenon. Incisura must be distinguished from the two normal incisura seen in the bismuth-filled stomach, the incisura cardiaca and the incisura angularis previously mentioned. A deep peristaltic contraction, seen only on the plate, may be mistaken for an incisura.

*Duodenum.*—By expression of the water-bismuth in the manner previously mentioned the superior horizontal portion of the duodenum, the bulbus duodeni, or cap, is visualized. Ordinarily it shows as a small cone with its base directed downward and separated from the stomach by the pyloric ring. It is subject to variations in size, position, and outline. Normally regular, it may be



distorted by ulcer, of which it is a common seat. Bands of adhesions from the gall-bladder may produce irregularities or displace it, usually upward. The first portion of the duodenum, having a smooth inner wall, shows a regular outline when filled with bismuth. The second and third portions show the inward projections of the valvulæ conniventes.

The normal duodenum empties itself with great rapidity. Residue from the bismuth-water or pap may remain proximal to a stenosis from ulcer or adhesions or from spasm. Residue in the cap may or may not be of significance. The residue here spoken of should not be confounded with the residue from the six-hour Rieder meal previously discussed, although this also may rarely be seen in the duodenum. The duodenum normally empties itself so quickly that the bismuth-water is merely glimpsed on the screen in passing and rarely shows on the plate. When the bismuth-water tarries long enough to visualize the duodenum throughout for a minute or so, or is held at any point long enough to outline itself definitely on the screen or appear on two or three plates, I am accustomed to speak of it, a little loosely, perhaps, as residue. In such cases the duodenum may sometimes be seen either on the screen or plate as a three-quarters circle, an appearance not infrequently seen in duodenal ulcer. Residue may accumulate proximal to a stenosis from ulcer or adhesions or from reflex spasm, or from kinking at the duodenojejunal juncture.

Quite commonly the cap is vertically above the pylorus, especially in "fish-hook" stomachs, and with the patient in a standing position bismuth tends to collect in the cap, simply by means of gravity, sometimes in a thin, disk-like layer above the pyloric ring. With "steer-horn" stomachs the cap is often in the horizontal axis of the stomach and no disk-like residue accumulates in it. A kink at the duodenojejunal juncture may be evidenced by residue in a dilatation proximal to it. Perforating duodenal ulcer has been found with a diverticulum, similar to that of gastric ulcer. A tender pressure-point on the duodenum may assist in arriving at a diagnosis of duodenal ulcer, but is not necessarily pathognomonic, and its importance should not be overestimated.

*Jejunum*.—When filled with bismuth, the jejunum shows its wave-like valvulæ. Outlines are indistinct. Peristalsis is active, and masses of bismuth are pushed forward rapidly at intervals.

*Ileum*.—Somewhat irregular in its upper half by reason of its valvulæ, the ileum becomes smooth and regular in its lower portion. Its terminal loop commonly dips into the pelvis and ascends to join the cecum at an acute angle. Here it may be narrowed by pericecal adhesions, particularly from appendicitis. There is a tendency for bismuth to collect in the terminal coils of the ileum, and opinions as to obstruction here should be cautious.

### THE COLON

*Size*.—It is to be remembered that the average colon diminishes in diameter from the cecum to the sigmoid. While the cecum and ascending colon are relatively larger than the rest of the bowel, they are sometimes abnormally dilated as a result of fecal stasis. The descending colon is frequently quite narrow, with sharply marked haustra. The length of the colon varies considerably in individuals, and redundancy of the sigmoid and descending or transverse colon is often encountered, especially in persons who complain of constipation.

*Position*.—Eccentricities of position most frequently seen are ptosis of the transverse colon, usually accompanied by redundancy, and displacement upward or downward of the cecum. Non-rotation of the cecum is an abnormality occasionally observed, the entire colon occupying the left side of the abdomen. The splenic flexure is least subject to alteration of position.

*Patency*.—Obstruction to the inflow of the opaque enema may be observed on the screen. If due merely to spasm, this soon relaxes. A tumor may have a narrow central channel, proximal to which the colon again shows its normal breadth. Filling defects about the cecum, due to adhesion-producing inflammation, are not uncommon. Fecal scybala may produce apparent filling defects in the colon. Marked spastic narrowing for a considerable distance is quite often seen, especially in the descending colon and sigmoid. Usually information can be gained from the opaque





enema regarding external fistulas. Diverticula have been diagnosed by this means.

*Mobility.*—Most of the colon is accessible to palpation, and abnormal variations in mobility can thus be determined while screening. This is of especial value in the cecal region, where the normal mobility of the cecum may be greatly restricted by adhesion.

*Peristalsis.*—The examiner will rarely see peristaltic action. Opinions have differed as to whether the analward movement of the colonic contents is by infrequent but rapid propulsion in mass, or by slow vermicular progression, or both.

*Ileocecal Valve.*—In a fair proportion of cases the opaque enema will go beyond the valve into the ileum. Whether this incompetence has any pathologic significance is yet to be decided.

*Appendix.*—Now and then the enema fills the appendix, visualizing its lumen and giving some information of its length and position. Bismuth is slowly evacuated from it, and traces may remain for days.

#### SIGN GROUPS

The various diagnostic indications above discussed may be synthesized into sign complexes. For example, the radiologic evidences of gastric ulcer comprise:

1. The diverticulum of perforating ulcer.
2. Visualization of the bismuth-filled crater of a callous ulcer.
3. The incisura, or transverse contracture, indenting the greater curvature.
4. Localized-pressure tender point on the lesser curvature.
5. Residue after six hours.
6. Acute "fish-hook" form of the stomach, with displacement to the left and down.
7. Delayed opening of the pylorus.
8. Settling of the bismuth to the lower pole of the stomach, such as is seen in hypotonicity or atony.

The Roentgen-ray signs of gastric cancer include:

1. Filling defects.
2. Diminution in size.
3. Lessened mobility.
4. Stiffening and gaping of the pylorus, as shown by a free and continuous outflow of bismuth from the stomach.
5. Absence of peristalsis from affected portions of the wall of the stomach.
6. Antiperistalsis.
7. Residue after six hours, if the pylorus is obstructed, or, on the other hand,
8. If the pylorus is unobstructed, hypermotility, with early clearance of the stomach and an advanced position of the six-hour meal in the intestine.

In duodenal ulcer there may be:

1. Early free opening of the pylorus, with early clearance of the stomach.
2. Lagging of bismuth in the duodenum.
3. Residue in the stomach (sometimes in the duodenum) after six hours there is an obstruction from scar contraction.
4. Pressure-tender point over the duodenum.
5. Dilatation of the cap.
6. Irregular outline of the cap or duodenum.
7. Diverticulum of perforating ulcer.
8. Vigorous peristalsis, especially if there is obstruction.

Radiologic diagnosis of duodenal ulcer, unless corroborated by clinical data, is in most instances a mere guess. Excluding obstructive cases, the Roentgen-ray appearance of duodenal ulcer is often seen when the actual lesion is elsewhere, as in the appendix or gall-bladder.

#### INTERPRETATION OF THE PLATE

Discussion of the relative superiority of the screen or the plate is useless. There is no competition between them. Each serves certain purposes. Both are necessary for satisfactory gastro-intestinal work.

The plate gives a permanent record. It gives finer detail, and permits longer and closer study of minutiae than does the screen. Stereoscopic plates are especially interesting and valuable in many instances.

Recording, as it does, a single momentary phase of the contractions, interpretation of the plate must be guarded. Compression of the stomach between the spine and the plate may produce apparent filling defect of the pyloric end of the stomach or even apparent hour-glass. Incessant systole and diastole of the antrum make it appear vague and indefinite on the plate.

Bismuth poorly suspended may settle irregularly and give rise to the appearance of filling defects on the plate. What seems on the plate to be kinks, narrowings, or obstructions of the small large intestine are very rarely such. Even serial plates have this element of uncertainty.

Mobility, peristalsis, the presence or absence of deformities, filling defects, or incisura, must all be determined by the screen examination, during which every phase of movement may be seen.

27. PATENCY--rFree dDilated (C. Not Seen, I. Normal, 2. Adhes. 3. Vagueness.) mMkd. mMkd.  
 28. PERISTALSIS--(0 1 2 3).....oObstructed sSlightly Vagueness.  
 29. BULB--nRegular dDeformed Size..(1 2 3 4).....rResidue (1 2 3 4).....oNot Seen  
 (C. A. (indicat. Full of Lungs, Small Affected) S. D. S)  
 30. PATENCY--nNorm dDilated .....oObstructed.....by kKink sSpasm aAdhesion tTumor bForeign body fFistula vDiverticulum

JESUNUM

27. PATENCY--fFree dDilated oObstructed sSlightly mMild.  
(n. Not Seen, 1. Normal, 2. Active, 3. Vigorous.)
28. PERISTALSIS--(0 1 2 3).....
29. BULB--nRegular dDeformed Size..(1 2 3 4).....rResidue (1 2 3 4).....oNot Seen  
(C, A, H, F, T, S, F, D, S)  
(Indicate Part of Large Bowel Affected)
30. PATENCY--nNorm dDilated.....oObstructed.....by kKink sSpasm aAdhesion tTumor bForeign body fFistula vDiverticulum
31. PERISTALSIS--nNorm rRapid sSlow fFrequent iInfrequent
32. COMPETENCE--iIncompetent oObstructed
33. VISIBILITY--vVisible
34. LUMEN--nNorm wWide rNarrow tTortuous cCurled kKinked fFistula
35. POSITION--nNormal dDisplaced rRt. lLft. uUp dDown  
(n. Fixed, 1. Slightly Mobile, 2. Mobile, 3. Very Mobile.)
36. MOBILITY--(0 1 2 3).....
37. PATENCY--nNormal iDilated.....oObstructed.  
(n. Not Seen, 1. Normal, 2. Active, 3. Vigorous.)
38. PERISTALSIS--(0 1 2 3).....aAntiperistalsis
39. MISCELLANEOUS--vDiverticulum.....uFistula.....jJackson's M.....rRedundancy.....sFilling Defect.  
xNon-Rotation.....aAnomaly.....bForeign Body.....
40. OBSERVATION--after iInjection gIngestion
41. PATENCY--fFree dDilated oObstructed by iImpaction tTumor bForeign body aAdhesions fFistula
42. TEST BREAKFAST--Chemical; tTotal Acidity.....fFree Hcl.....cCombined Acidity.....lLactic Acid.....Microscopic;  
bBlood.....rFood Remnants.....sSarcinae.....yYeast Cells.....
43. ANTISPASMODIC--Given yYes nNo
44. SPECIMEN PHOTOGRAPHS--yYes nNo
45. PREVIOUS OPERATIONS.....
46. OPERATIVE FINDINGS.....

46. REMARKS:

Fig. 22.





the patient can be turned about for vision at different angles, and the effect of palpation may be noted.

#### METHOD OF RECORDING FINDINGS

At intervals during the screen examination the observer or his assistant hastily notes on a scratch sheet the more important facts elicited, together with any striking features of the anamnesis. Most of this is easily done by checking or underscoring the appropriate item. The form which I show here (Fig. 21) also provides for the gastric analysis, which findings are usually entered beforehand. Making notes while screening is rather trying to the eyes, and I have occasionally used a dictagraph.

From a comparison of the screen findings with the plates the final conclusions are drawn. These are entered, mostly by underscoring, on the permanent record sheet here illustrated (Fig. 22). The small letter before an underscored item is entered in its proper column on a recapitulation-sheet, from which information can be readily derived for statistical purposes, but it also promotes thoroughness of observation by its constant reminders.

Visualization of a cancer of the stomach with obvious filling defects, or a gastric ulcer with a characteristic incisura or a niche is so dramatic that the exuberant enthusiasm thus aroused has unfortunately created the impression in some quarters that the Roentgen-ray is ready to supersede the ordinary clinical methods of diagnosis. This impression should be discouraged, for in the vast majority of instances the Roentgen-ray is only a link in the chain. The Roentgen-ray is not a rival of clinical methods, but a most valuable adjunct thereto, and worthy of routine employment.

To maintain a proper conservatism in the interpretation of roentgenologic findings is difficult, yet absolutely necessary. We should remember, among other things, that only a very small percentage of those who complain of gastric symptoms have gastric lesions.

Roentgenologists have reason to be proud of the tremendous advances which have been made in the radiology of the digestive tract, but it behooves them to be careful that the record shall not

be marred by overenthusiasm or by long lists of conclusions drawn from short lists of cases.

The Roentgen-ray findings, unless extraordinarily marked and decisive, should be correlated with the anamnesis, the laboratory reports, the clinical data, and always with common sense. There are cases of ulcer and cancer of the stomach and obstruction of the bowel in which the combined fluoroscopic and skiagraphic findings are of themselves sufficiently determinative to justify a diagnostic opinion. But there is a greater number of cases in which the combined *x*-ray examination will merely elicit suspicious or even only eccentric appearances, a percentage of these being due to real lesions, a larger percentage accompanying only functional disturbances. Here opinions should be advanced with the greatest caution, and the final diagnosis should rest on all the evidence obtainable from every source. This necessitates an extensive correlation, a broad knowledge based on experience, and a careful judgment.

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## THE ROENTGEN-RAY AS AN AID IN THE DIAGNOSIS OF GASTRIC CANCER AND ULCER \*

R. D. CARMAN

In a paper on "The Operative Treatment of Cancer of the Stomach" read before the Section on Obstetrics, Gynecology and Abdominal Diseases, American Medical Association, Minneapolis, June, 1913, W. J. Mayo stated that "The early diagnosis of cancer does not depend on any sign or symptom due to cancer itself, but on the mechanical conditions produced by the growth. Therefore, in cases of suspected cancer of the stomach the recognition of such mechanical conditions should be the first aim of the diagnostician." In enumerating the signs and symptoms he has placed first the presence of a palpable tumor in 67 per cent.; second, food remnants in 53.3 per cent., and, third, the Roentgen-ray.

The work of the last few months at the Mayo Clinic with the Roentgen-ray has necessitated a change in the order of importance of these signs, the Roentgen-ray showing diagnostic signs in 93 per cent. of the cases. This fact is very encouraging, as it will mean an earlier diagnosis with earlier surgical interference and a higher percentage of cures. In gastric ulcer the radiologic diagnosis is less certain, but even here approximately 65 per cent. show diagnostic signs, and this percentage will probably be materially increased in the future.

A discussion of the numerous and varied technics† now used in

\* Read before the Indiana State Medical Association, September 24-25, 1913. Reprinted from the Journal of the Indiana State Medical Association, November 15, 1913, pp. 495-505.

† In a recent paper I acknowledged the debt we owe to Rieder, of Munich, who, in 1904, first used an opaque salt (bismuth subnitrate) in the Roentgen-ray examination of the human gastro-intestinal tract. While the records indicate this to be

the radiologic examination of the digestive tract would here be superfluous, but a brief description of our present routine, on which the following observations are based, is necessary for clarity.

#### TECHNIC

Having taken an ounce of castor oil the evening before, the patient reports in the morning without breakfast. He is then given an ordinary portion of breakfast cereal into which 2 ounces of barium sulphate has been well mixed, together with a little sugar and cream. He is directed to abstain from further food until after the examination and to return six hours later. He is then stripped down to the hips; the screen is placed against the abdomen and the presence or absence of residue in the stomach from the morning meal noted.

The patient now drinks rapidly 6 or 8 ounces of water containing 2 ounces of bismuth subcarbonate, well stirred. Its entrance and descent into the stomach are carefully watched. When all has been drunk, the observer palpates toward the pylorus, and is often able to drive a quantity through into the duodenum, thus visualizing it. He then presses the bismuth in the stomach upward, watching the outline of the greater and lesser curvatures.

Sixteen ounces of potato-starch pap\* containing 2 ounces of bismuth subcarbonate and flavored with syrup of raspberry is then drunk by the patient. Usually this fills the stomach quite well, outlining it clearly. Irregularities which may have been previously observed with the bismuth water are palpated to determine their nature and permanence. Mobility and peristalsis are also determined. Plates are then made, the patient standing with his abdomen against the plate-holder, with the upper edge of the plate at or near the nipples.

true, my attention has again been directed to the fact that, seven years previously, Cannon employed bismuth in his investigations on animal digestion, thus establishing the priority of an American in this field.

\* This is made with potato starch (or potato flour), which can be bought at any grocery store for ten cents a package. For making a pap of creamy consistence one or two tablespoonfuls is dissolved in 6 or 8 pints of water, brought to the boiling-point, and allowed to cool. If too thick, more water may be added. If too thin, more potato starch is needed. It is then filtered through a tea strainer to remove all lumps.

After the observer becomes familiar with his technic, has followed a large mass of material to operation, and acquired confidence through confirmation of his diagnoses, he will find that prolonged examinations are neither necessary nor desirable. Our total screening time for a patient very rarely exceeds five minutes, and

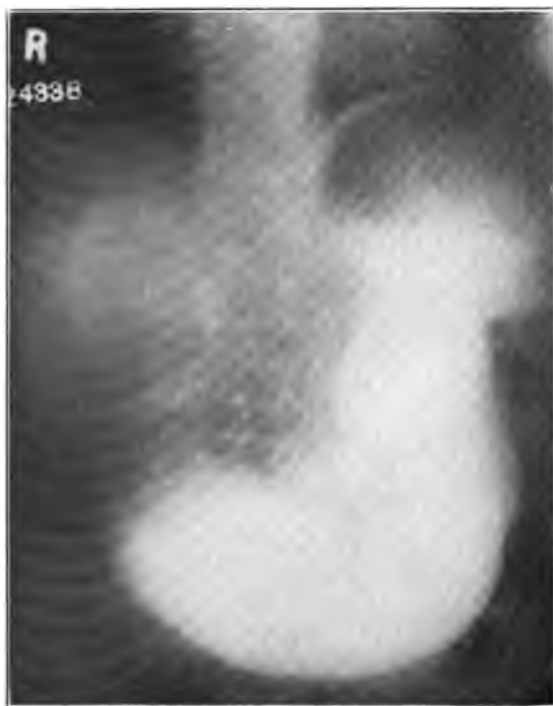


Fig. 23.—(Case No. A 90,713; X-ray No. 24,338.) Male, aged sixty-seven years. X-ray findings: Rather large stomach with active peristalsis. Slight irregularity at pyloric end, which is slightly obstructed. Operative findings: Early carcinoma; irregular, indurated growth on posterior wall, extending to pyloric ring, 5 x 2 x 2½ cm.

in the majority of cases the screening is finished within two or three minutes, because signs of gastric lesions revealed by the Roentgen-ray are relatively gross, readily seen, and appear quickly or not at all. Errors in diagnoses are due more often to seeing too much rather than seeing too little, and this sort of error is apt to be the consequence of a lengthy inspection. Besides, with long study

of a case, the observer tends to lose his sense of proportion—the little things are emphasized at the expense of the big ones.

The Roentgen diagnosis of gastric lesions is based on departures from the normal form, tonus, position, motility, capacity, mobility, contour, and peristalsis of the stomach, together with certain extraordinary phenomena, such as filling defects, incisura, and diverticula.



Fig. 24.—(Case No. A90,713; X-ray No. 24,338.) Residue after six hours.

A better understanding of abnormal conditions will perhaps be aided by a condensed review of the normal appearance.

#### THE NORMAL STOMACH

As to form, two general types of stomach are met with, the steer-horn and fish-hook. The steer-horn, as the name implies,

has some resemblance to the horn of a steer, being broadest at its base or upper pole, the cardia, and narrowing toward the pylorus, which is its most dependent portion. This type is relatively infrequent, and when found, usually occurs in association with a deep chest and broad costal arch, such as is seen occasionally in muscular men and more rarely in women.

The far more common fish-hook type is usually less narrowed in its pyloric portion than the steer-horn, has a more uniform width, and its midportion is more dependent, resulting in a J or



Fig. 25.—(Case No. A90,713; X-ray No. 24,338.) Pyloric end of stomach laid open, showing early carcinoma just within pyloric ring. (See skiagrams, Figs. 23 and 24.)

hook shape. It occurs in nearly all women and in many men, and is found almost invariably wherever the habitus enteroptoticus of Stiller is found.

Tonus is a measure of the ability of the gastric musculature to maintain tonic contraction. The orthotonic, or normal toned, stomach grasps its contents firmly and hence is of tubular form, whether the amount of ingesta be large or only moderate. Exaggerated, diminished, and absent tone are designated respectively as hypertonic, hypotonic, and atonic. The hypertonic, usually

of the steer-horn type, occasionally the fish-hook, is not only of small diameter, but is short and held well up in the abdominal cavity. The hypotonic is rather broad at its lower pole and the bismuth tends to settle below the cardia. The atonic stomach, seen only rarely, hangs as a flaccid bag with a basin-like lower pole;



Fig. 26.—(Case No. A83,494; X-ray No. 21,020.) Male, aged thirty. Marked filling defect greater curvature, pars media. No residue. Gaping pylorus. Exploration: Carcinoma of the stomach.

the walls of the lower cardia and upper media are more or less apposed, and the gas-bubble is fusiform in shape.

The position of the stomach depends somewhat on its form and tonus. The steer-horn is high and obliquely placed. Its lower border is well above the umbilicus. The cardia and media of the fish-hook stomach usually hang almost vertically, the pyloric por-



tion curving horizontally to the right and then upward. Its lower pole is at or near the umbilicus. In either form the normal position of the pylorus is assumed to be about an inch above and an inch to the right of the umbilicus.

The motility of the stomach is its emptying power. The time



Fig. 27.—(Case No. A83,132; X-ray No. 20,801.) Male, aged forty-one. Filling defect on lesser curvature. No residue after six hours. Pylorus gaping. Operation: Carcinoma of stomach.

of evacuation depends, of course, on the character of the food, carbohydrates making their exit earlier and proteids later. Experience has shown that failure of the stomach to clear itself of certain barium or bismuth salts within six hours is indicative of a pathologic condition.

Twenty-four to 30 fluidounces (720 to 900 c.c.) of ingesta will

fill the average adult stomach without discomfort. A capacity markedly less or markedly greater than this is usually abnormal.

The stomach is fixed only at its cardiac and pyloric ends. Between these points it should be quite freely mobile to palpation.

The gastric contour is normally regular, being broken only by

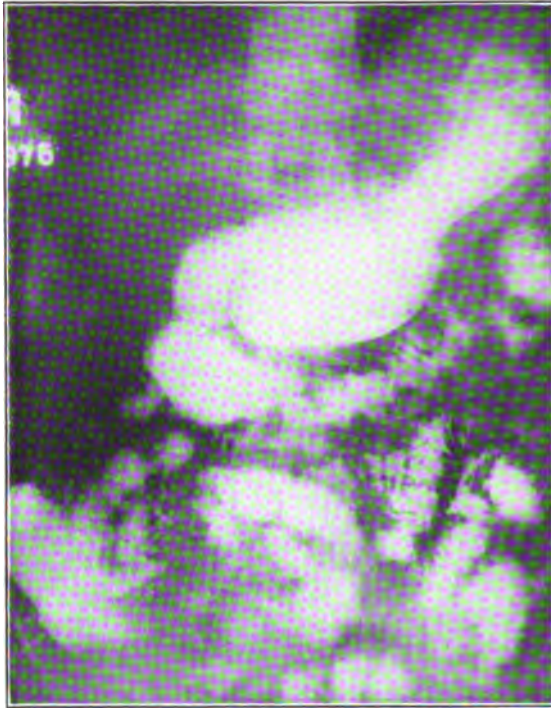


Fig. 28.—(Case No. A89,707; X-ray No. 23,875.) Female, aged 33. Filling defect especially in the pars media and cardiaca. No residue. Pylorus gaping. Exploration: Inoperable carcinoma of stomach.

the incisura cardiaca, a slight indentation on the greater curvature below the cardia, the incisura angularis, a deeper depression on the lesser curvature at the proximal limit of the vestibule, and by peristaltic waves. The gas-bubble shows as a semi-elliptic, sometimes fusiform, transparent area in the cardia above the level of the esophageal opening.

On the greater curvature a peristaltic wave begins as a shallow depression at the incisura cardiaca, which grows deeper as it progresses to the vestibule. On the lesser curvature the wave is deepest and traverses a short distance from the cardia to the incisura angularis, which it replaces. The vestibule disappears by



Fig. 29.—(Case No. A90,077; X-ray No. 24,021.) Female, aged fifty-six. Filling defect and irregularity especially of the pars media extending well up in cardia. No residue. Exploration: Inoperable carcinoma.

concentric contraction and is immediately succeeded by a new vestibule.

#### CANCER

The radiologic signs of carcinoma of the stomach I would arrange in the order of their relative importance as follows:

1. Filling defects.

2. Altered pyloric function. (a) Gaping of the pylorus. (b) Obstruction of the pylorus.
3. Advanced position of the six-hour meal.
4. Absence of peristalsis from involved areas of the wall of the stomach.
5. Diminished mobility; loss of flexibility.



Fig. 30.—(Case No. A83,115; X-ray No. 20,799.) Female, aged sixty-two. Radiogram shows "fish-hook" stomach with a moderately large projection on the lesser curvature. Small residue after six hours. Operation: Resection one-half middle of stomach; end-to-end union. Pathologic report: Carcinomatous ulcer with glandular involvement.

6. Diminution in size of the stomach.
7. Antiperistalsis.

The filling defect is a sign of cardinal import and practically indispensable in the Roentgen-ray diagnosis of carcinoma. It is occasioned by the projection of the tumor mass into the lumen of the stomach, and when filled with bismuth the visualized contour

of the gastric lumen shows a corresponding irregularity. Obviously, filling defects vary in size according to the extent of involvement. They also vary in appearance somewhat, according to the character of the cancer. The encephaloid (medullary) carcinoma produces large, usually multiple, irregularities, while



Fig. 31.—Case No. A86,077; X-ray No. 22,288. Male, aged fifty-seven. Stomach markedly contracted, showing filling defects in its lower third. Marked involvement of the posterior wall obstructing the cardia. Note bismuth in esophagus. Exploration: Extensive carcinoma of the stomach.

in the scirrhus type the indentations are very small, even absent, although the concentric narrowing may greatly lessen the caliber of the stomach, especially at the pyloric end, and give it a funnel or retort form, also diminishing its capacity. Invasion of the media by the growth may result in a marked hour-glass stomach, the loculi being united by a more or less tortuous canal.

True filling defects must be carefully differentiated from indentations of the wall of the stomach by a gas-filled colon, by adjacent extrinsic tumors, notably those of the liver, spleen, colon and mesentery, and by spasm. The splenic flexure, in spite of preparation by purging, will often be distended with gas and give

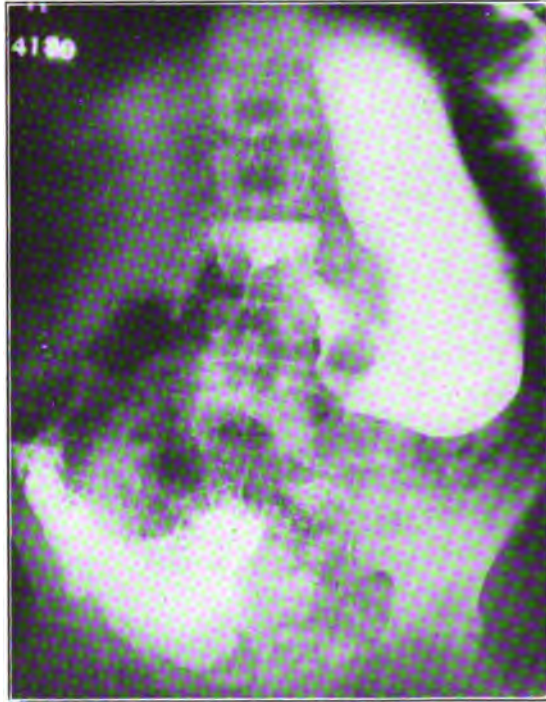


Fig. 32.—(Case No. A90,280; X-ray No. 24,130.) Female, aged fifty-two. Radiogram shows filling defect or irregularity of the pars media and pylorica. No residue after six hours. Operation: Carcinoma; three-fifths of the stomach resected.

the adjacent greater curvature of the stomach a somewhat ragged aspect. By palpation during the screen examination the stomach can be pushed away from the colon, causing this raggedness to disappear, or at least show its character. Filling defects caused by tumors external to the stomach deforming its contour are less easily differentiated. However, such filling defects may change

in appearance with slight palpation, or even with respiratory movement. During the screen examination the intimate relation of a palpable tumor-mass to the stomach and its correspondence to a filling defect in the gastric outline may sometimes be determined. The deformity produced by spasm, most often the hour-glass, is

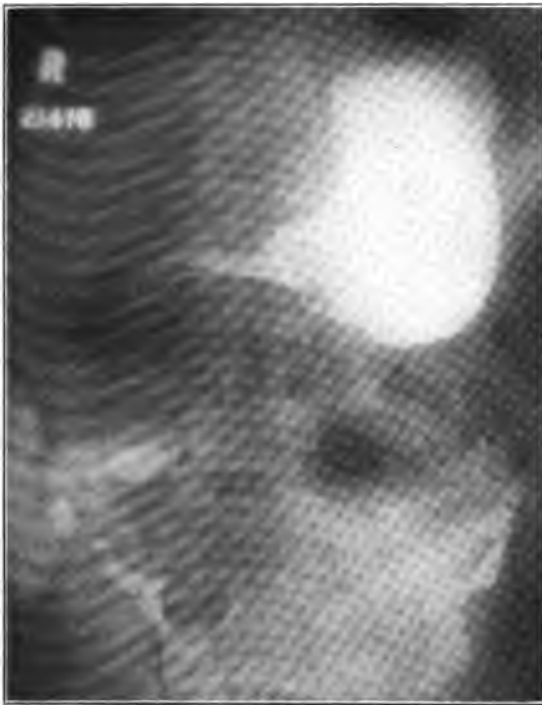


Fig. 33.—(Case No. A84,287; X-ray No. 21,415.) Male, aged forty-three. Radiogram shows filling defect at pyloric end. No residue after six hours. Operation: Carcinoma of the stomach.

sharply delineated, in contrast with the usually indefinite shadings of a tumor-produced filling defect. Frequently it relaxes on energetic manipulation. Antispasmodics, such as belladonna, given for two or three days prior to a second examination, will generally cause such a spasm to disappear.

In the cardia a filling defect may deform the normally regular

gas-bubble, the tumor outline showing more or less clearly. Examination of the patient recumbent, in which position the cardia is more completely filled with bismuth, may show such filling defects in stronger relief.

Alteration of the pyloric function is an almost invariable accompaniment of gastric carcinoma, and may reveal itself in either



Fig. 34.—(Case No. A83,026; X-ray No. 20,738.) Male, aged seventy. Pyloric end of stomach fixed and obliterated. Large residue after six hours. Operation: Carcinoma.

of two quite opposite ways, namely, free and continuous patency or marked obstruction.

In the carcinomatous stomach the pylorus, whether because of actual stiffening by infiltration or by reason of lessened acidity of the gastric contents, often remains gaping and the bismuth ingesta flow freely and continuously through it.



On the other hand, pyloric obstruction, varying in degree with the situation and size of the tumor, is also a common result of cancer. It is evidenced by a distinct, often large, residue from the six-hour meal.

Obstruction may occur at any point in the lumen from the



Fig 35.—(Case No. A90,500; X-ray No. 24,236.) Male, aged sixty-one. Radiogram shows filling defect in pars pylorica. Residue after six years. Operation: Carcinoma; three-fifths of stomach resected.

cardia to the pylorus. An hour-glass stomach may show a six-hour residue in its upper loculus. High obstruction tends to dilatation of the esophagus, which may be quite marked in obstruction at the cardia. If there be no obstructive condition, the "head," that is to say, the most advanced portion of the six-hour meal in the intestines, will occupy a position more or less proportionate to

the degree of acidity. Ordinarily at or near the cecum after six hours, it may be accelerated by the hypoacidity incident to carcinoma of the stomach. In such cases it may be found anywhere from the hepatic flexure to the rectum, quite commonly in the transverse colon or at the splenic flexure. While this phenom-



Fig. 36.—(Case No. A90,500; X-ray No. 24,236.) Residue after six hours.

enon is, strictly speaking, only a gross measure of the acidity, it is an item of corroborative value.

The peristalsis of a carcinomatous stomach often shows certain departures from the normal. Peristaltic vigor is generally proportionate to the degree of acidity, and as diminished acidity is a common accompaniment of carcinoma, we often find in this latter condition a notable diminution in force and frequency of the

peristaltic waves. However, in the case of recent pyloric obstruction the effort at compensation may show itself in quite vigorous contractions.

More important is the interruption of peristaltic waves by carcinomatous infiltrations. A wave will progress to the affected area, skip it, and take up its course beyond.



Fig. 37.—(Case No. A84,005; X-ray No. 21,276.) Male, aged thirty-six. Marked cutting off pyloric end of stomach with irregularity. Marked residue after six hours. Operation: Freely movable tumor size of small hen's egg at pylorus, causing almost complete obstruction. Another tumor on lesser curvature. Anterior gastro-enterostomy. Either carcinoma or syphilis. Wassermann positive. Pathologic report: Tissue removed inflammatory.

Lessened mobility occurs sufficiently often as a result of carcinoma invading adjacent structures, thus more or less fixing the stomach, to justify its inclusion among the important signs of cancer. Not rarely the fixation is extreme, and energetic manipulation will fail to alter the position of the stomach.

Aside from lessened mobility en masse there may also be a notable loss of flexibility of the wall of the stomach, such that ordinary palpation has little effect on its contour.

Antiperistalsis, *i. e.*, peristalsis in the reverse direction, has been noted in carcinoma by some radiographers.



Fig. 38.—(Case No. A83,327; X-ray No. 20,934.) Male, aged fifty-five. Filling defect or irregularity of the pars pylorica. Residue after six hours. Exploration: Carcinoma of the stomach.

Accurately speaking, of course, the question of malignancy is for the pathologist to determine with finality. However, the filling defects of carcinoma of the stomach are so characteristic radiologically that these cases can be diagnosed as such in 93 per cent.

With reasonable care and a decent regard for the clinical facts, the Roentgen-ray findings will not only markedly enhance the

percentage of correct diagnoses of cancer, but will also often furnish valuable information as to the advisability of operative intervention. For example, extensive involvement of the cardia, or of the media and cardia, renders surgical measures hopeless, while pyloric carcinoma offers a better prospect for surgical intervention, especially if there be no metastasis.



Fig. 89.—(Case No. A90.102; X-ray No. 24,023.) Female, aged fifty-two. Filling defect pars pylorica. No residue. Diagnosis: Ulcer or carcinoma. At operation: Gross ulcer with perforation lesser curvature just above pylorus.

### ULCER

The radiologic signs of gastric ulcer may be classified in two groups: (a) Those which are cardinal and more or less pathognomonic; (b) those which are merely suggestive.

The cardinal signs are as follows:

1. Visualization of the bismuth-filled crater of a callous ulcer (the nischen symptom).
2. The diverticulum of perforating ulcer.
3. The incisura.

Signs which are not determinative but merely suggestive of ulcer include:



Fig. 40.—(Case No. A86,058; X-ray No. 22,280.) Male, aged forty. Filling defect pars media and pylorica. No residue after six hours. Pylorus gaping. Exploration: Carcinoma of the stomach.

1. Acute fish-hook form of the stomach with displacement to the left and down.
2. Delayed opening of the pylorus.
3. Localized pressure-tender point on the lesser curvature.
4. Residue in the stomach after six hours.
5. Lessened mobility.

6. Settling of the bismuth to the lower pole of the stomach, such as is seen in hypotonicity or atony.

A bud-like projection from the contour of the bismuth-filled stomach, corresponding to the crater of a calloused ulcer, is a definite and valuable sign. It will usually be on the lesser curva-

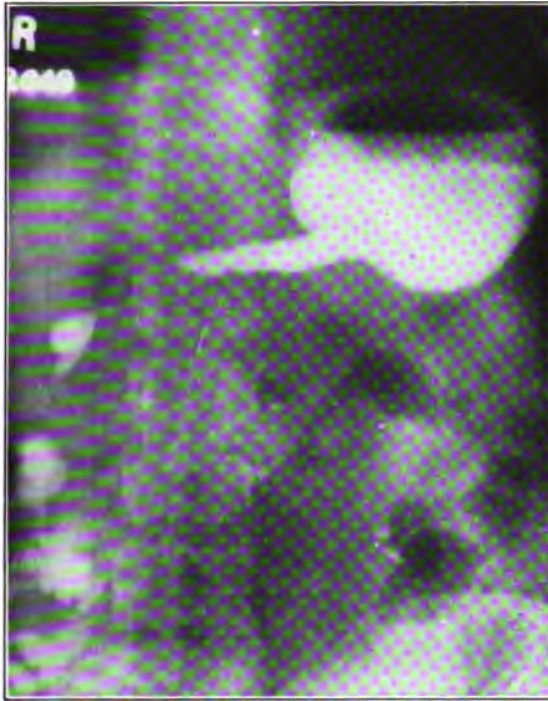


Fig. 41.—(Case No. A86,914; X-ray No. 22,649.) Male, aged sixty-one. Filling defect pars media and pylorica with contraction. Residue after six hours. Exploration: Extensive carcinoma of the stomach.

ture when found, is rather easily recognized, and is not imitated, at least closely, by any other condition that I know of.

The diverticulum of perforating ulcer is quite as characteristic. The perforation may be anterior into the liver or posterior into the pancreas, and a continuation of the ulcerative process results in an excavation, which, when visualized with bismuth, shows a rather

regular, often spheric, outline. Those that I have seen ranged in size from a filbert to a walnut. A diverticulum sometimes shows as a miniature stomach just outside the stomach's outline, with a lower layer of bismuth and a median layer of fluid, capped above by an air-bubble. Frequently it will retain bismuth after



Fig. 42.—Stomach removed postmortem, filled with bismuth, and radiographed. Note thickness of walls and narrowing of lumen due to the invasion of a colloid carcinoma. It gives a radiogram such as is shown in Fig. 41.

the stomach is empty. Whether the diverticulum is in the liver or pancreas may commonly be determined. If in the pancreas, rotation of the patient causes a wider excursion on the screen than if it is in the liver. If in the liver, the diverticulum moves with respiration, while that in the pancreas does not. An oblique view will also show the more posterior situation of the latter.



Organic hour-glass contraction of the stomach usually, but not invariably, accompanies diverticulum. Commonly the canal joining the two segments is short and near the side of the lesser curvature. Organic hour-glass is differentiated from spasmodic or functional hour-glass by the persistence of the former after en-



Fig. 43.—(Case No. A80,973; X-ray No. 19,835.) Female, aged forty-four. Radiogram shows a fish-hook stomach. No residue after six hours. It shows a small projection on the lesser curvature, which is the bismuth-filled crater of a callous ulcer and a marked transverse contraction of the greater curvature (incisura) opposite this niche. Operation: Excision of ulcer on lesser curvature about 5 inches from pylorus, with surrounding fibrous tissue; gastroduodenostomy. Pathologic report: Gastric ulcer, scar tissue.

ergetic palpation, or after the administration of belladonna for two or three days. Both these procedures, however, may fail occasionally to relax a spasmodic hour-glass.

Organic hour-glass stomach may also occur in penetrating ulcer without diverticulum.

The incisura is an indentation of the greater curvature, usually

in the vertical portion of the stomach, pars cardiaca or pars media, of varying width and depth. Its production is believed to be due to the irritation of the ulcer causing a spastic contraction of the circular muscle-fibers in its plane, perhaps in some cases also due to infiltration and stiffening of these fibers.



Fig. 44.—(Case No. A90,906; X-ray No. 24,376.) Female, aged forty-nine. Note marked indentation of greater curvature, with a projecting niche on lesser curvature. Residue after six hours. Operation: Ulcer of the stomach.

A true incisura is distinguishable from a peristaltic wave, not only by its depth, which is commonly greater than that of a peristaltic contraction, but also by the fact that it does not move pylorus-ward. It persists in spite of vigorous palpation, and is not effaced after the administration of belladonna to the patient.

Pressing the lower pole of the stomach upward by palpation

will often cause the gas-filled splenic flexure to indent the greater curvature, particularly at the costal arch. This should not be mistaken for an incisura. The latter will show when the stomach hangs naturally.

A slight depression on the greater curvature, at the juncture of the cardia and media, the so-called "incisura cardiaca," is seen in



Fig. 45.—(Case No. A77,396; X-ray No. 18,393.) Female, aged 54. Hour-glass stomach, fish-hook type, displaced to the left, extending below umbilicus, showing diverticulum just outside stomach outline on lesser curvature. Diverticulum contained bismuth after the upper loculus had emptied. Diagnosis: Diverticulum due to perforating ulcer of the stomach. Operation: Perforating ulcer of stomach, perforating into the liver.

most stomachs, and should not be confounded with the pathologic incisura.

Incisura often have a high situation on the greater curvature. As ulcerous stomachs are frequently hypotonic, the bismuth may settle below the level of the incisura and thus fail to visualize it, with the patient standing.

Incisura are sometimes seen after giving the bismuth water which disappear on filling the stomach with the bismuth pap. Whether these are merely transient reflex spasms, or whether they are real incisura which are effaced by the great weight (25 to 30 ounces) of bismuth ingesta, is an unsettled question. To



Fig. 46.—(Case No. A30,520; X-ray No. 18,993.) Female, aged thirty-four. Screen showed fish-book" stomach with a transverse contraction (incisura) on the greater curvature which persisted under palpation. Owing to rapid settling of the bismuth below the level of the incisura plates were made with the patient prone in order to show the incisura well. To eliminate the possibility of spasm, atropin was administered for two days. Re-examination shows the incisura still present. Diagnosis: Ulcer of the lesser curvature. Operation: Excision of ulcer, size of a quarter, high up on lesser curvature, adherent to pancreas. Pathologic report: Simple ulcer

obviate the possible effect of weight and of bismuth settling below the level of an incisura or spasm, examination in the recumbent posture may be of service.

False incisura occur not infrequently in which no ulcer or other organic lesion is found. They are probably due to spasm from reflex causes. In appearance they resemble true incisura, but

they often move pylorusward, and usually disappear on palpatory manipulation, or after the administration of an antispasmodic.

These tests are ordinarily decisive, but I have lately seen a case in which a persistent, apparently genuine incisura was found at operation to be due to a mesenteric band passing over the



Fig. 47.—(Case No. A87,715; X-ray 23,007.) Male, aged thirty. Irregular filling defect pars media. Marked bulging lesser curvature. Residue after six hours. Active peristalsis. Duodenum contains bismuth. Operation: Ulcer of the duodenum. Thick callous perforating ulcer lesser curvature, perforating into pancreas; many adhesions.

greater curvature and attaching to the hepatic flexure, thus constricting the stomach. No ulcer was present.

A hypotonic stomach of an acute fish-hook form, with displacement to the left and down, is not uncommonly associated with ulcer, as a result of scar contraction on the lesser curvature drawing

the pylorus to the left. The contraction may be extreme, resulting in Haudek's "snail form."

Delayed opening of the pylorus following the administration of bismuth water, apart from actual pyloric obstruction, is almost invariably seen in ulcer of the stomach associated with hyperacidity.



Fig. 48.—(Case No. A78,465; X-ray No. 18,813.) Male, aged fifty-two. Radiogram shows small projecting mass on lesser curvature with slight contraction opposite on greater curvature, which was seen moving toward pylorus. Operation: Ulcer 4 inches above pylorus on lesser curvature, most extensive on anterior wall, with a callus the size of a silver dollar, actual crater the size of a nickel. Resection in continuity.

This delayed opening is also frequently seen as a reflex from disease of the gall-bladder or appendix.

A residue from the six-hour meal may or may not be found in cases of ulcer. It has occurred in about 70 per cent. of the cases that we have examined so far. The amount varies from a small fraction up to a quarter or more of the meal. In some cases the

residue is probably due to spasm of the pylorus, but an invasion of the pylorus by the ulcer may produce actual obstruction. In our cases, six-hour residues were usually found with the perforating types of ulcer, but were rarely seen with callous or simple ulcers.

The presence of a localized pressure-tender point on the lesser curvature is not very trustworthy as an indication of ulcer at that



Fig. 49.—(Case No. A88,239; X-ray No. 23,248.) Female, aged fifty-three. Incisura in pars media, greater curvature. No residue. Diagnosis: Ulcer of the stomach (the diagnosis being based on the incisura, which persisted after the administration of belladonna). Operation: Appendectomy. Division of Lane's kink. Incisura due to an adhesive band which extended from the jejunum to the hepatic flexure.

point. Many persons who have no ulcer are sensitive to pressure in the epigastrium. Further, clinicians assure us that unless the parietal peritoneum is involved (as in penetrating ulcer, for example), visceral lesions are not particularly painful to pressure. However, such a tender point, if definitely localized, is entitled to consideration in the final summing up.

A hypotonic condition of the stomach, with settling of the bismuth to the lower pole, while by no means constant in ulcer, is found sufficiently often to warrant its inclusion among the suggestive signs.

Notwithstanding the numerous cardinal and suggestive radio-



Fig. 50.—(Case No. A81,588; X-ray No. 20,112.) Male, aged forty-one. Filling defect lesser curvature, pyloric end. Diagnosis: Former gastro-enterostomy functioning; filling defect due probably to carcinoma. Confirmed at operation.

logic signs of ulcer, there is a small percentage of cases in which these signs are either absent or too indefinite to support a diagnosis. This is especially true of non-perforating ulcers in the pars pylorica, and on the anterior and posterior walls, and the shallow or superficial ulcers which are of relatively frequent occurrence.

From what has been said it may be gathered that at present



none of the Roentgen-ray signs of cancer or ulcer is pathognomonic. The relative value of those signs, singly or in groups, can be learned only by experience. Nor should the diagnosis rest on them alone. The Roentgen-ray simply furnishes valuable contributory evidence as to the presence and nature of gastric lesions—so valuable that whenever available it should be routinely employed



Fig. 51.—(Case No. A87,716; X-ray No. 23,008.) Male, aged forty-two. Hour-glass stomach with projecting mass on lesser curvature in pars media. Small residue in projecting mass and large residue in lower loculus after six hours. Operation: Perforating ulcer.

—but the final judgment should take into account all the evidence of every sort.

Hence, the radiologist should be not only a radiographer, but a clinician to the utmost of his ability; he should study his cases from the clinical side, follow them to the operating-table, and take his rightful share of responsibility.

The radiology of gastric lesions is still young, and with en-



Fig. 52.—Case No. A89,922; X-ray No. 24,631. Penetrating ulcer with diverticulum. Hour-glass stomach.

thusiasm in the work and conservatism in adjudging the results, it will take still higher rank among diagnostic measures.

# THE PATHOLOGIC EVIDENCE OF THE RELATIONSHIP BETWEEN GASTRIC ULCER AND GASTRIC CANCER \*

LOUIS B. WILSON

Pathologists, clinicians, and surgeons are still in disagreement as to the relationship of gastric ulcer and gastric cancer. So much of this disagreement as does not rest on the inherent conflict of preconceived ideas which are found to be in opposition to new observations are usually based on—(1) Failure to understand the pathologic data; (2) inappreciation of the bearing of the clinical data; or (3) failure to appreciate the correlation existing between the two.

To these three factors I wish to call your attention.

## PATHOLOGIC DATA

In examining a small ulcerated area from the stomach—say, not over 5 mm. in diameter—which has but little induration in either border or base, the pathologist is safe in diagnosing the lesion as simple gastric ulcer. When he is examining a portion of the stomach containing a large, cauliflower-like mass on a thickened base with at most only small, irregular, shallow ulcers involving only the mucosa and showing evidence of only recent necrosis, the pathologist is warranted in saying, from the gross appearance alone, that there is probably no evidence in the specimen of ulceration previous to cancer formation. When examining a portion of the stomach which contains a large ulcerated area with a thickened base and an indurated overhanging border, no path-

\* Read before the St. Joseph County Medical Society, South Bend, Indiana, November 21, 1913.

ologist can tell from the gross specimen whether or not the case is simple ulcer plus cancer or cancer without convincing evidence of previous ulceration. In other words, many specimens resected from the stomach are of such a character that it is impossible to determine from their gross appearance what may be their pathologic histology. The pathologist thus, so far as the examination of the gross specimen is concerned, is but little better off than is the radiographer who draws his conclusions from a shadow of the gross lesion; or than the analyst who sizes up the situation from what he finds the gland units of the stomach may be doing; or than the internist who hazards a diagnosis from his interpretation of the patient's and his own sensations.

The microscopic examination of the tissue from an ulcerated gastric lesion gives us evidence of chronic and acute processes occurring in both the connective tissue and in the epithelial elements of the organ. It is our interpretation of the relationship of the two processes in these two structural elements upon which rests our ability to say whether or not the process was primarily one of ulcer, with subsequent development of carcinoma, or whether it was primarily carcinoma with subsequent ulcerative necrosis of portions of the neoplasm.

Whether or not chronic ulcer of the stomach is always primarily the result of an infective process, as is most likely true, there can be no question but that after a lesion of the mucosa once occurs, from whatever primary cause, it must always become infected. When such an infection has once begun, the process extends by necrosis not only laterally, but also in succession to and through the several coats of the stomach. Accompanying the necrosis of tissue nature constantly attempts to repair the injury by local leukocytosis, by the deposition of fibrin, by the formation of granulation tissue, and, finally, by the formation of scar tissue.

It is evident that in the ulcerative process the mucosa is destroyed before the submucosa and other layers of the gastric wall in the base of the ulcerated area. Thus we find in the base at the center of a simple ulcerative process no evidence of normal epithelium. When, however, the ulcerative process extending later-

ally creeps around portions of the mucosa, segregating it into islets of epithelium, these latter atrophy and lose their normal appearance. Thus, while we find regularly in the base of the simple ulcers no epithelial element, we do quite as regularly find in the spreading border of such ulcers many islets of epithelium more or less segregated from the normal expanse of gastric mucosa and more or less atrophic.

Nature attempts in the stomach, as elsewhere, to check the advancing border of the necrotic lesion by bringing thereto not only phagocytes, but also excessively large amounts of nutriment, which stimulates to overgrowth both the structural and the epithelial elements, producing a thick, raised margin, consisting not only of hyperplastic connective tissue, but also of hypertrophic and hyperplastic epithelium.

When the process of necrosis is checked, the process of regeneration advances. Thus there is a tendency to cover the surface of the scarred base of an ulcer with more or less well-differentiated epithelium. This reparative process very rarely is complete. Indeed, it is doubtful if ever, once the adult mucosa has been completely destroyed, that there is developed completely functioning epithelium on the scar-tissue base.

The development of a gastric cancer consists essentially in the overgrowth of the mucosal epithelium in an aberrant manner. The new epithelial cells are imperfectly developed, they do not form normal gland elements with normal functions, nor are they normally placed. Hence at the first glance it would seem to be a simple matter to diagnose most sharply, from the histologic standpoint, the two processes of ulceration and cancer formation. Such, however, is not the case, for unfortunately we have shrunken, irregularly shaped and irregularly placed epithelial cells in the borders of simple gastric ulcers, and also in the borders of such ulcers we have hypertrophic and hyperplastic overgrowths of epithelium which we have insufficient evidence to show are malignant in character. On the other hand, we find in gastric carcinomas epithelial cells which have been surrounded by fibrous connective tissue and so pressed upon and cut off from their nutrition that

they no longer exhibit the characteristics of that exuberant overgrowth which marks them when seen alone as carcinomatous.

Thus, in gastric lesions of undoubted ulcerative character it is necessary that we determine the presence of epithelial cells out of their proper places and bearing evidence in themselves of exuberant growth and of incomplete differentiation in order to make a positive diagnosis of carcinoma. Because of the indecisive character of such data there remains a group of cases about which there must always be doubt in the mind of the pathologist as to whether or not the histology gives sufficient evidence to warrant a diagnosis of carcinoma.

The diagnosis of cancer of the stomach once having been made, our determination of the supervention of cancer on previous ulcer depends upon our interpretation of the relationship between the regressive and progressive changes present. All pathologists agree, on the one hand, that when we have, in a large lesion, evidence of ulcerative involvement of the mucosa and submucosa, or, better yet, of the other layers of the gastric wall as well, in the base of which lesion there exists only scar tissue, we are warranted in assuming that the lesion in this area was one of primary ulceration. On the other hand, when within the bases of such ulcerated areas there are found epithelial elements of undoubted cancer characteristics, it is impossible to say positively that they have not supervened on a previous ulcerative lesion, and when, on examining a scar-tissue base, there are found nests of shrunken, degenerating epithelial cells, the evidence that they are degenerating carcinomatous cells is about as strong as that they are islets of degenerating normal epithelium. Thus, it would appear that in large ulcerative lesions of the gastric wall we have three groups of cases: first, a group which we may safely designate as ulcer preceding cancer; second, a group in which the evidence is insufficient on which to base such a positive statement, though it is strongly presumptive; and third, a group in which the evidence of previous ulceration, though suggestive, must always remain doubtful.

Having now defined the data on which we base our presumptive evidence from a pathologic standpoint, of the supervention of

gastric cancer on gastric ulcer, let us examine the pathologic facts afforded by our cases in the Mayo Clinic.

My first study of the pathologic relationship of gastric ulcer and gastric cancer, published four years ago was based on the examination of material from 210 stomachs. Forty-seven of these were ulcers without suspicion of cancer, 2 were sarcoma, 2 adenoma, and 1 was a diverticulum. There thus remained specimens from 158 cases, in 5 of which, though ulcer, there was enough microscopic appearance of epithelial tissue to place them in the doubtful class as possible beginning cancer. The remaining 153 cases were undoubted cancer, and of these, 71 per cent. presented pathologic evidence which we interpreted at the time as suggesting the presence of ulceration prior to the development of cancer.

MacCarty has recently reported the result of his observations, mostly on gross specimens and on sections of fresh tissues, of the relationship of gastric ulcer and gastric cancer in some 600 specimens, about one-fifth of which were simple chronic ulcers. He summarizes his findings as follows:

"First, single and multiple chronic gastric ulcers occur with all the characteristics of simple ulcers plus the presence of carcinomatous cells in their borders, minus the presence of similar cells in the bases." "Second, single and multiple gastric ulcers occur which present the microscopic characteristics of simple ulcer plus the presence of carcinoma in the borders and bases, but with glandular involvement and metastases.

MacDowell and Simpson have recently compiled the data and prepared the tissues for microscopic study of those cases from which specimens were removed from the stomach or duodenum, whether at operation or autopsy, in the Mayo Clinic from January 1, 1905, to November 15, 1913. This covers a total of nearly 900 cases, and includes a review—(1) of all cases reported in 1909; (2) of all cases reported by MacCarty, 1913; (3) a large proportion, though not all, of the cases reported by Smithies, 1913,\* and (4) a number of cases occurring in 1913 and not included in any of

\* Dr. Smithies' series contained some cases on which the diagnosis was based on the clinical picture, supplemented by the surgeon's findings at operation, but from which no tissue was removed.

these lists. These cases are now being studied in detail by MacDowell and myself. While our observations are still incomplete, they have reached a stage from which we may compile approximately accurate statistics.

Of the 827 cases from which tissue has been studied, 42 were inflammatory without definite ulceration (syphilis, tuberculosis, etc.), 17 were benign tumors, 4 were sarcomas, 279 were ulcers without the presence of cancer, and 485 showed cancerous tissue. Of these 485 cases, the specimens from 206 showed ulcer with cancer in the border and none in the base, while in approximately half of the remaining 279 cases the specimens were of more doubtful structure, that is, there were some proliferating epithelial cells around the borders of the base combined with cancer of the overhanging edges of the ulcer. Thus in between 60 and 70 per cent. of the cases it is fair to say that there was found more or less pathologic evidence pointing to ulcer formation with scar-tissue base prior to the development of proliferating epithelium in the area now occupied by the border of the ulcer, while in from 30 to 40 per cent. of the cases such evidence is absent or inadequate. That there is an evident reduction in the percentage of gastric cancers, with evidence of previous ulceration being resected in this clinic, a diminution from 71 per cent. prior to 1909 to a little above 50 per cent. in 1913—is no doubt due to the fact that a much greater percentage of patients with advanced gastric cancer, but with long histories of gastric ulcer, now are given gastric resections rather than palliative gastro-enterostomies as in preceding years. In these very advanced cases all pathologic evidence of preceding ulceration has usually disappeared.

#### CLINICAL DATA

The most important data from the clinical standpoint for regarding cancer of the stomach as having developed on preceding ulcer is a history given by the patient, extending over several years, which, taken by itself, is indistinguishable clinically from histories given by other patients whom operation or autopsy shows to have been affected with gastric ulcer only. And, further, that this his-



tory of ulcer has been succeeded by a history, lasting through a few months only, which is indistinguishable clinically from histories in other patients who at operation or autopsy have shown the presence of gastric cancer.

Graham's attention in the later nineties was strongly attracted by the many long histories of "dyspeptic" trouble that preceded cancer of the stomach, and the thought that this precancerous condition was ulcer became firmly implanted. Graham further says: "In eliciting the history of gastric cancer there are three types found: (1) Those in which the initial symptoms were slight and a long latent period has intervened; (2) those in which the acute symptoms seem suddenly to attack the patient in the very midst of health; and (3) those with long series of repeated attacks which are evidently precancerous. In the first and third the precancerous history is that of ulcer."

Graham noted that "in 1905 a little less than one-half (47 to 49 percent.) of the cases had histories ranging from three to thirty-seven years' duration. If we add those of two years' standing, the percentage reaches 61."

Smithies has recently taken the clinical symptom-complex considered gastric ulcer by Friedenwald, and the clinical symptom-complex considered cancer by Osler and McCrae and applied these two clinical tests to 566 consecutive cases proved to be gastric cancer at operation in the Mayo Clinic. This, of course, involved the reconsideration of the histories of these cases with the definite symptom-complex of ulcer as defined by Friedenwald and of cancer as defined by Osler and McCrae in the mind of the reviewer. It was, of course, impossible in such a study to exclude entirely the personal equation of the reviewer, since the interpretation of the histories as written of a given series of cases would not be exactly the same by all observers even when they were measured by the same descriptive standards. However, even after we have allowed for such a personal equation on the part of Smithies, we find his conclusions broad enough in their teachings to make them of importance. The following is a summary of his article:

"Symptom-complex taken to mean gastric ulcer (Friedenwald).

Gastric malnutrition between ten and seventy years of age characterized by periodic or continuous abdominal discomfort or pain, frequently bearing relation to food ingestion and often associated with epigastric or dorsal tenderness, vomiting, loss of blood and of hyperacid gastric contents.

"Symptom-complex taken clinically to indicate primary gastric cancer (Osler and McCrae). A gastric malfunction of downwardly progressive nature, occurring between forty and seventy years of age, characterized by abdominal distress or pain, associated with cachexia, loss of blood, epigastric tumor, vomiting, and with gastric contents which reveal motor defects, low free hydrochloric acid, organic acids, and foreign microorganisms." When these two measures are applied to the 566 proved cases of gastric cancer, 239, or 42 per cent., fall into the cancer-following-ulcer group, while 182, or 32 per cent., are in the "primary" cancer division. There is, in addition, a group of cases of irregular ulcer that numbers 106, or 19 per cent., 22 cases, 4 per cent., that had a previous clinical history of gall-bladder affection, while 17 cases, or 3 per cent., had early symptoms pointing to primary processes in the appendix, the pancreas, or the bowel. Combining the returns from the two ulcer groups, it seems that precancerous history indicates that about 60 per cent. of the subsequently demonstrated cases of cancer gave earlier clinical evidences which we associate with chronic gastric ulcer prior to the time when the ailment assumed the clinical picture that we associate with gastric cancer."

Smithies further notes that the average length of time of all symptoms in our 182 cases clinically satisfying the symptom-complex of cancer alone was seven months, while of the 239 cases clinically satisfying the symptom-complex of chronic gastric disorder previous to the period of evident malignancy the average duration of symptoms was 11.4 years. In this group the average duration of the supervening malignant course was six months. It is thus manifest that the periods of downward progression (gastric cancer) closely approximate in the two classes of cases, *i. e.*, those that are primary cancer and those which follow gastric ulcer, and

that wholly independent of the earlier gastric history of the individual.

After gastro-enterostomy for chronic ulcer where the ulcer has not been excised, the individual rarely develops gastric cancer. We have had but four such cases which later developed gastric cancer following gastro-enterostomy for ulcer. Though this seems to be a strong presumptive argument against the proposition that cancer develops on preceding ulcer, we must remember that in the presence of a gastro-enterostomy the entire physiology of the stomach and the related viscera has been greatly changed by the establishment of drainage. We should recall also that in cases of gastric cancer in which no pyloric obstruction is demonstrable, gastro-enterostomy seems to grant a longer lease of life than when such an operation has not been performed.

Duodenal ulcer of the indurated type is a relatively commoner affection than gastric ulcer, yet duodenal cancer is a rarity. Why does not cancer of the duodenum occur more frequently? We do not know. But we do know that in the duodenum there is some protective mechanism against malignancy. In all our series only 4 cases of gastric cancer have been found which began on the gastric side and passed to the duodenum by direct extension, though the number beginning on the gastric side and passing up to the pylorus is very large. The duodenum is relatively free from the intense acidity and associated peptolytic power of the gastric juice, and drainage within it is at all times almost perfect.

#### CORRELATION OF PATHOLOGIC AND CLINICAL DATA

Of the 530 cases of gastric tumor that have come to operation or autopsy, the clinical diagnosis was *gastric ulcer* in 46 cases in which the pathologic diagnosis was *cancer on ulcer*; the clinical diagnosis was *ulcer* in 32 cases in which the pathologic diagnosis was *cancer* without sufficient evidence of previous ulceration; of the cases clinically diagnosed *cancer on ulcer*, the pathologic diagnosis was *cancer* without evidence of previous ulceration in 21 cases, but there was exact agreement between the clinical and pathologic diagnoses of *cancer on ulcer* in 235 cases. Clinical diag-

noses of *gall-stones* were made in 11 cases on which the pathologic diagnosis was *cancer on ulcer*, and in 2 cases on which the pathologic diagnosis was cancer; the clinical diagnoses were doubtful in 32 cases which pathologically were *cancer* and in 28 cases which pathologically were *cancer on ulcer*.

The most striking thing about this correlation of clinical and pathologic diagnoses which were made wholly independent of each other is the fact that the two were in agreement in their diagnoses in more than 80 per cent. of the cases. Such a parallelism when the clinician and the pathologist were reasoning from wholly different data and each entirely in ignorance of the other's conclusions cannot be explained as a mere coincidence.

#### SUMMARY

1. The most numerous chronic lesions of the stomach pathologically are in three well-defined groups: (a) Chronic ulcers; (b) lesions in all respects like those in Group A, except for the additional presence of carcinomatous areas in the borders; and (c) lesions carcinomatous throughout. Only a small number of cases are of doubtful classification (transition stages).

2. Of the specimens showing cancer, about 60 per cent. are in group *b* (ulcers with bases free of cancer), and about 40 per cent. in group *c* (cancers throughout).

3. About 60 per cent. of all cases of gastric cancer operated on in the Mayo Clinic give a long history (average, 11.4 years) of chronic gastric distress, preceding a short history (average, six months) of severe symptoms pointing to gastric cancer. The remaining 40 per cent. of the cases give short histories (average, seven months) only, and those parallel with the histories during the final period of the cases with previous long histories.

4. When the clinical and pathologic diagnoses of cancer-on-ulcer are compared case by case, they are found to agree in above 80 per cent. of the cases. The 20 per cent. margin of disagreement is explained principally by—(a) Cases diagnosed clinically other than gastric; (b) cases diagnosed clinically *ulcer* but showing pathologically early cancer, and (c) cases diagnosed clinically

cancer on ulcer but with the cancer so far advanced that pathologic evidence of previous ulceration has been destroyed. Such parallelism between the clinical and pathologic diagnoses from independent data cannot be mere coincidence and probably limits the error of each to less than 10 per cent.

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# CHRONIC GASTRIC ULCER AND ITS RELATION TO GASTRIC CARCINOMA \*

REVIEW OF 684 SPECIMENS †

WILLIAM CARPENTER MACCARTY AND ALBERT COMPTON  
BRODERS

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The discussion which is going on in the literature over the question of whether or not gastric carcinoma develops on chronic gastric ulcer and regarding the percentage of chronic ulcers which "become" carcinomatous is, it seems to the writers, a discussion which is not only dealing with an unanswerable question with our present methods of investigation, but is doing a great deal of unnecessary harm to mankind by preventing rational treatment. Viewed from the standpoint of feasibility of scientific investigation, such discussion seems superfluous, for the following reasons: (1) No one has seen a chronic gastric ulcer in the process of development. (2) No one has been able to witness the stages of reaction to irritation through which the tissues of the gastric wall pass during the formation of ulcer or carcinoma. (3) No one has ever recognized carcinoma in the process of development any place in man or other animal. (4) Even the most skilful cellular pathologist cannot point out the line of demarcation between a simple hyperplastic cell of the mucosa of a simple chronic ulcer and a malignant hyperplastic cell of a chronic ulcer which is associated with carcinoma. (5) No one has experimentally produced a carcinoma.

\* Read before the Southern Minn. Med. Soc., Mankato, August 5, 1913. Also before the Kentucky Medical Society, September 2, 1913. Reprinted from *Archives of Internal Medicine*, 1914, vol. xiii.

† This number includes 218 specimens previously reported by MacCarty, at the meeting of the American Medical Association, June, 1909, and published in *Surgery, Gynecology, and Obstetrics*, May, 1910.

With these fundamental limitations upon our knowledge, one can only view the conditions as they occur. The known facts



Fig. 53.—(18088) Multiple chronic gastric ulcers in various degrees of extension.

which are seen in the specimens herewith presented are the following:



Fig. 54.—(18088) Gross section through four ulcers, showing the degrees of extension through the wall of the stomach.

(1) Single and multiple chronic ulcerations occur in the stomach (Figs. 53 and 54).

'13—11

(2) They vary widely in size (diameter and depth) (Figs. 53, 54, 57, 58, 60, 61, 62, 63, 65, 66, 70, 71, 81, 85).

(3) The characteristics of simple chronic gastric ulcers consist of excavations in the wall of the stomach, and these excavations may have the mucosa, muscularis mucosæ, submucosa, musculature, subserosa, or perigastric structures for their bases, depending upon their depth (Figs. 54, 89, 90).



Fig. 55.—(18088) Low-power photograph through the smallest ulceration in Figs. 53 and 54. The destruction has not extended through the muscularis mucosæ. Some distortion of the glands and lymphocytic infiltration of the mucosa.

(4) The excavations may be wide and shallow (Fig. 54) or narrow and deep (Figs. 60, 61, 89, 90).

(5) The mucosa of the borders of gastric ulcers may gradually recede from the base or overhang the base (Figs. 54, 66, 86).

(6) The epithelium of the mucosa, which is the most natural source of carcinoma, may be normal (differentiated) (Figs. 67, 68, 76) or hyperplastic (partially differentiated) (Figs. 74, 77, 78, 79),



or irregularly hyperplastic (undifferentiated) (Figs. 75, 76, 77), or irregularly hyperplastic and migratory (extraglandular or in the stroma) (Figs. 83, 84, 88).

(7) The bases of chronic gastric ulcers consist of scar tissue which radiates usually from the center of the ulcer or is perpen-

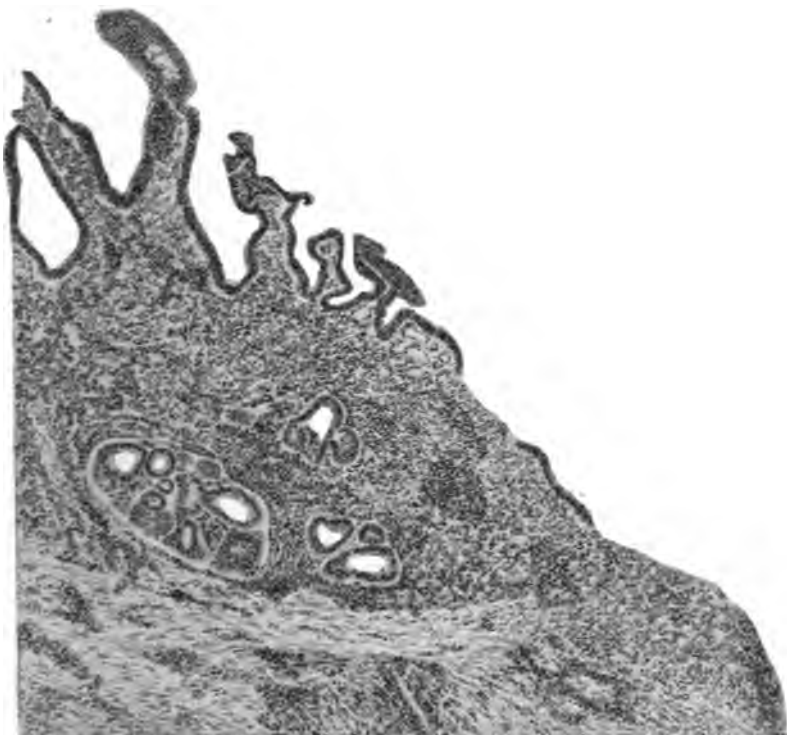


Fig. 56.—(18088) Low-power drawing through the wall and part of the base of the second smallest ulcer in Figs. 53 and 54. The destruction has extended through the muscularis mucosæ and into the submucosa. There are extensive distortion of the glands and lymphocytic infiltration.

dicular to the plane of the coats of the stomach (Figs. 59, 64, 72, 82, 87).

(8) Usually the surface of the base is composed of necrotic tissue, which is infiltrated with lymphocytes (Figs. 59, 64, 69, 72, 73, 82, 87).

(9) Carcinomatous cells occur in the lower parts of the mucosa and in the immediate submucosa, without their being present in the base (Figs. 82, 83, 84).

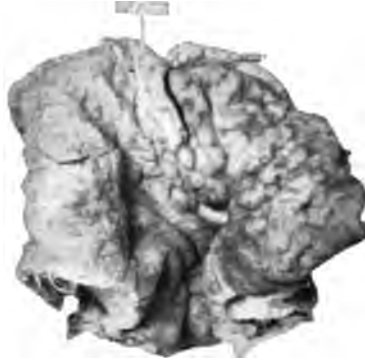


Fig. 57.—(28173) Single simple chronic gastric ulcer

(10) Of 684 specimens which were either excised or resected from the stomach, 191 were simple chronic ulcers or ulcers in which



Fig. 68.—(28173) Gross section through the ulcer in Fig. 57 shows the depth and extensive scar tissue of the base. The ulceration has extended through all the gastric coats.

no histologic evidence of carcinoma was present. There were 472 specimens which presented the characteristics of simple ulcer plus

the presence of carcinoma, and 21 specimens of ulcer in which the presence of cancer was doubtful. The ulcer which contains the smallest amounts of carcinomatous cells contains these in the mucosa of the borders and not in the base. The earliest carcinomatous condition of the cells is not seen in so-called "cut-off" epi-

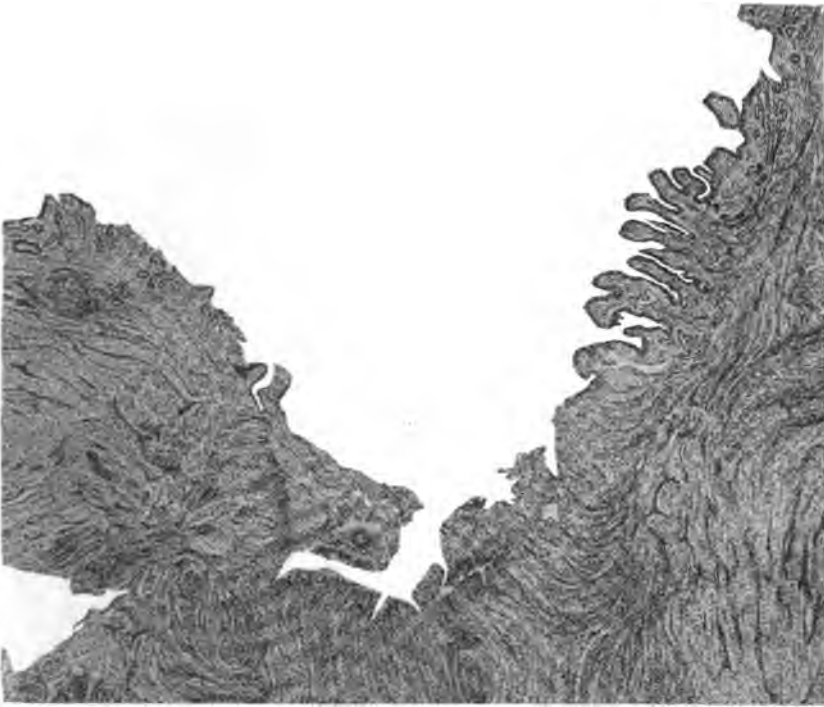


Fig. 59.—(28173) Low-power drawing through the specimen in Figs. 57 and 58, showing the characteristics of a single chronic gastric ulcer. Destruction, distortion of the mucosa, lymphocytic infiltration, necrosis of the tissue in the base, and the arrangement of the scar tissue in the base.

thelium, in scar tissue of the base, but is seen in the epithelium of the mucosa itself (Figs. 78, 79, 83, 84).

Without regard to clinical history, certain conclusions may be drawn from the facts enumerated above, *i. e.*:

- (1) Single and multiple chronic ulcers occur in the stomach.
- (2) Single and multiple chronic gastric ulcers occur with all the

characteristics of simple ulcers plus the presence of carcinomatous cells in their borders, minus the presence of similar cells in the bases.

(3) Simple and multiple gastric ulcers occur which present the macroscopic characteristics of simple ulcer plus the presence of carcinoma in the borders and bases, indeed, with glandular involvement and metastases.



Fig. 60.



Fig. 61.

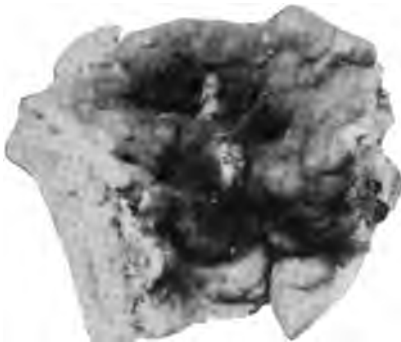


Fig. 62.



Fig. 63.

Figs. 60, 61, 62, and 63.—(37378 and 40640) Photographs showing simple chronic gastric ulcers.

The question for the clinicians and the surgeons is not, "Does gastric carcinoma develop on gastric ulcers, and what percentage of ulcers become malignant?" but, "Has the proved association of gastric carcinoma with chronic gastric ulcer sufficient significance to be of prognostic value in cases clinically diagnosed gastric ulcer?"

The association of these two conditions, in conjunction with the fact that the immediate operative mortality, the postoperative mortality, and the subsequent duration of life after gastric resection, bear a definite relation to the extent of the carcinomatous involvement,\* should be sufficient to stimulate a consideration on the part of every physician of the possibility of chronic gastric ulcers not only becoming but actually being carcinomatous.

The question of differential diagnosis in such cases may also be answered by facts, the most salient of which is the fact that the

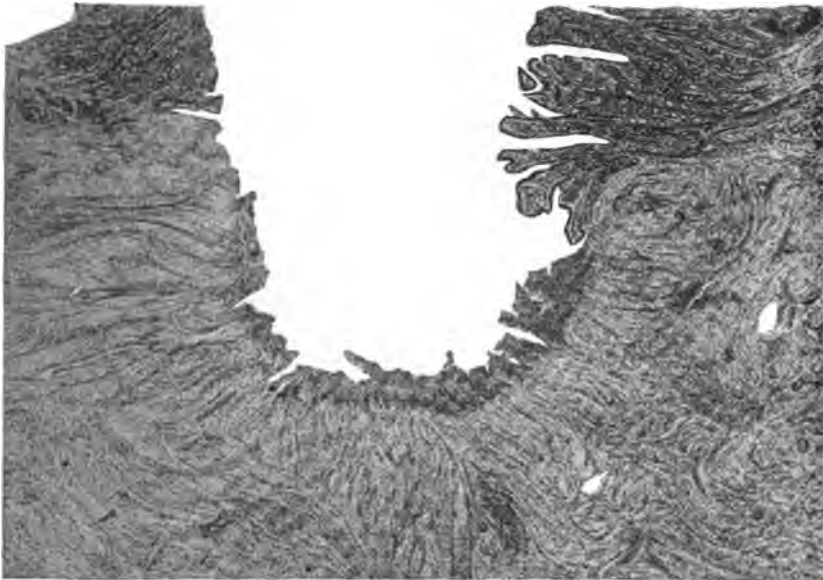


Fig. 64.—(27381) Low-power drawing, showing the characteristics of a simple chronic gastric ulcer.

differential diagnosis is often to be made only after removal by a cellular pathologist and not by the clinician or surgeon.

Do we know of any method other than exploration and microscopic examination which positively answers the question of whether or not a specimen inside or outside the body is carcinoma?

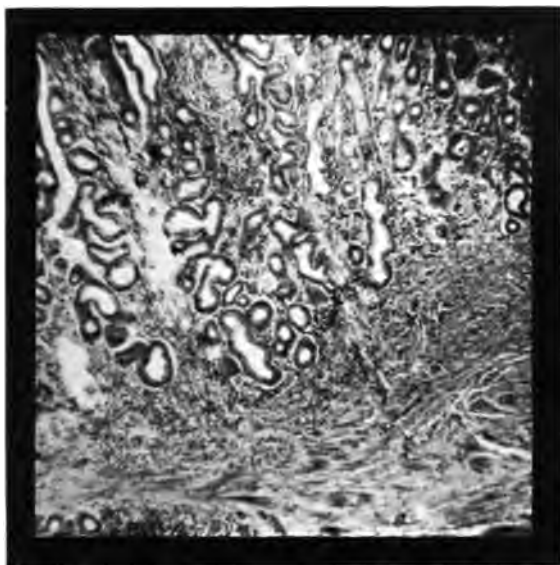
\* MacCarty and Blackford: "Involvement of Regional Lymphatic Glands in Carcinoma of the Stomach," *Annals of Surgery*, June, 1912, 811-843.



Figs. 65.—(49687) Photograph of a simple chronic gastric ulcer.



Fig. 66.—(49687) Photograph of a simple chronic gastric ulcer.



**Fig. 67.—(48401)** Low-power photograph, showing the character of the glands of the mucosa in a simple chronic gastric ulcer. The epithelium consists of definitely differentiated cells which still retain the characteristics of the usual gastric epithelium.



**Fig. 68.—(48401)** Low-power photograph, showing the character of the glands of the mucosa in a simple chronic gastric ulcer. The epithelium consists of definitely differentiated cells which still retain the characteristics of the usual gastric epithelium.



Fig. 69.—(48401) Low-power photograph through the base of a simple chronic gastric ulcer, showing lymphocytic infiltration and scar tissue.



Fig. 70.



Fig. 71.

Figs. 70 and 71.—(53453) Photographs of a simple chronic gastric ulcer.



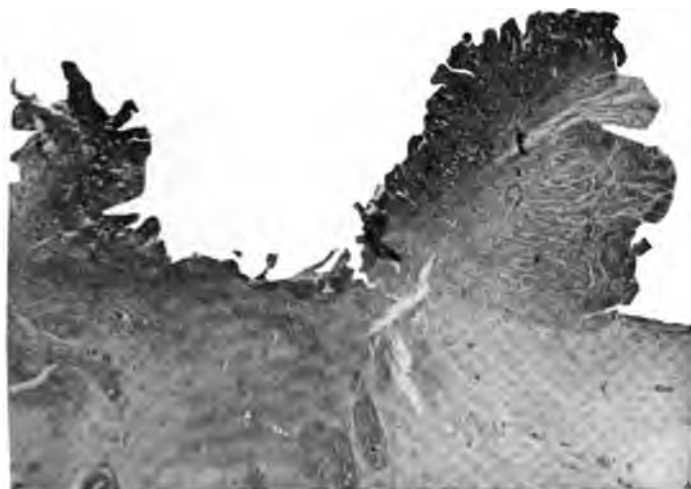


Fig. 72.—(53630) Low-power photograph through a simple chronic gastric ulcer

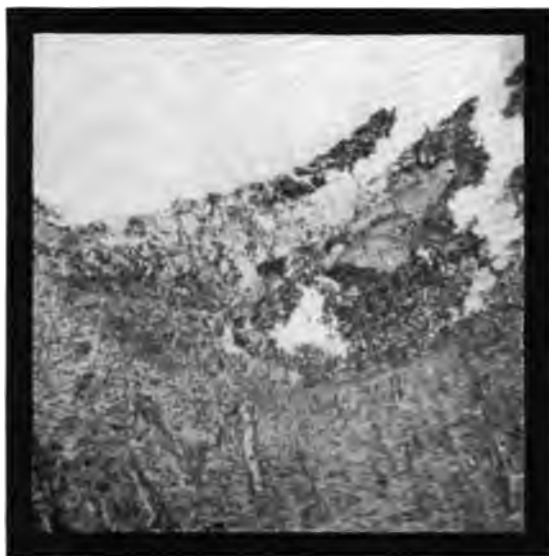


Fig. 73.—(53630) Low-power photograph through the base of the ulcer in Fig. 72.

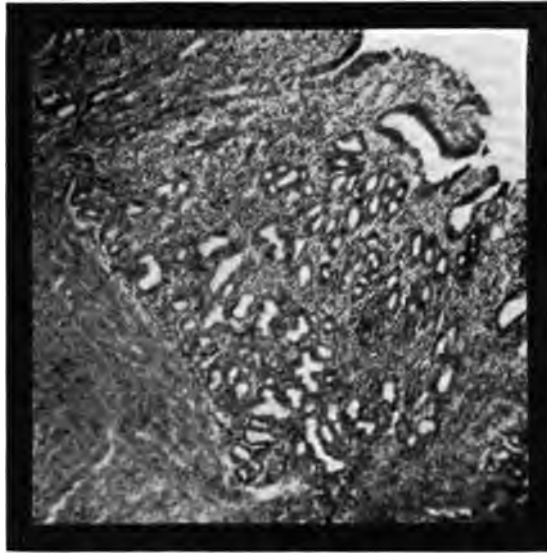


Fig. 74.

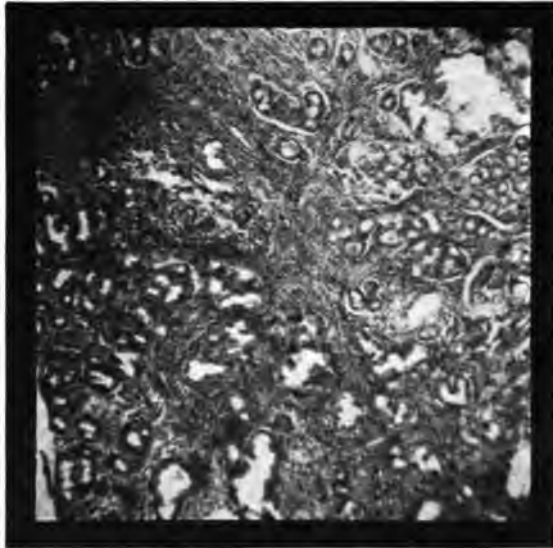


Fig. 75.

Figs. 74 and 75.—(53630) Photographs of the epithelium in the mucosa of the borders of a chronic gastric ulcer (Fig. 72). (The glands are more irregular than those seen in Figs. 67 and 68.) The cells are not as typically differentiated as those in Fig. 68, and still there is no definite invasion of the stroma. The cells resemble many of those which are seen in carcinoma (Figs. 83, 84, and 88).

The clinical history, gastric analysis, *x*-ray, and serum diagnoses cannot positively differentiate these groups of cases, especially those without pyloric obstruction. Indeed, the microscope, which is our

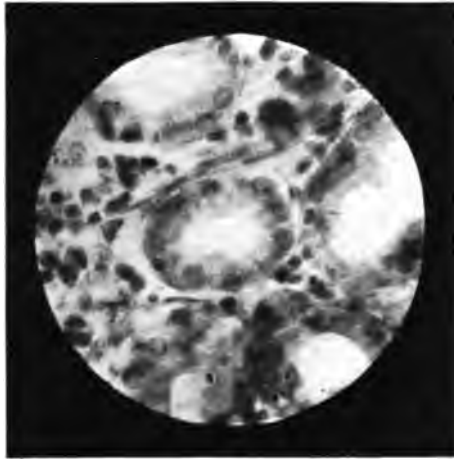


Fig. 76.

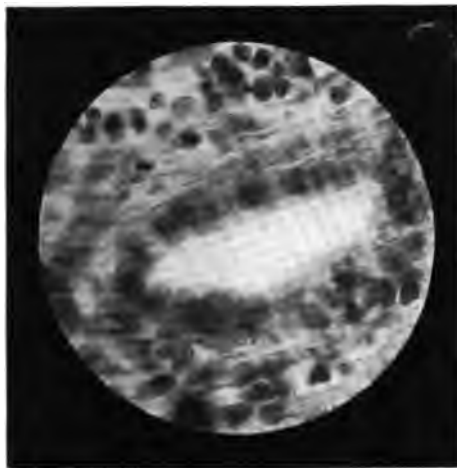


Fig. 77.

**Figs. 76 and 77.—(53630) Photographs of the epithelium in the mucosa of the borders of a chronic gastric ulcer (Fig. 72). (The glands are more irregular than those seen in Figs. 67 and 68.) The cells are not as typically differentiated as those in Fig. 68, and still there is no definite invasion of the stroma. The cells resemble many of those which are seen in carcinoma (Figs. 83, 84, and 88).**



Fig. 78.

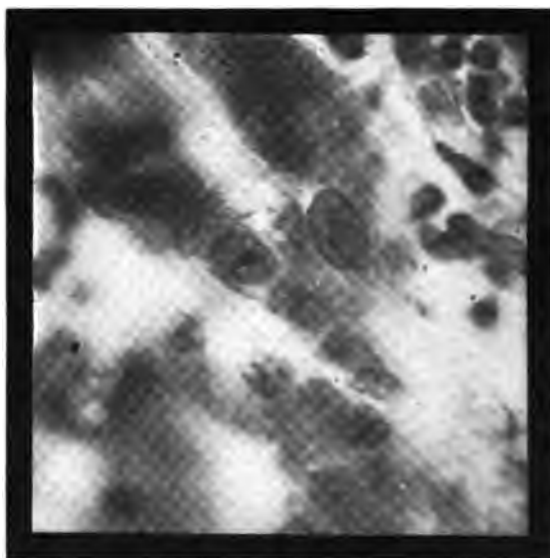


Fig. 79.

Figs. 78 and 79.—(53630) Photographs of the epithelium in the mucosa of the borders of a chronic gastric ulcer (Fig. 72). (The glands are more irregular than those seen in Figs. 67 and 68.) The cells are not as typically differentiated as those in Fig. 68, and still there is no definite invasion of the stroma. The cells resemble many of those which are seen in carcinoma (Figs. 83, 84, and 88).



**Fig. 80.—(35572) Photograph through a chronic gastric ulcer.**



**Fig. 81.—(35572) Photograph through chronic gastric ulcer.**

present highest court of appeal, can do no more than to divide the specimens into three groups, namely, simple ulcer group, carci-



Fig. 82.—Low-power photograph through the ulcer which is seen in Figs. 80 and 81. The characteristics of simple chronic gastric ulcer may be seen to exist. There is no carcinoma in the base.



Figs. 83.—(35572) Photograph of undifferentiated, irregular epithelial cells in the submucosa, just below the muscularis mucosae. The cells are typical of carcinoma.

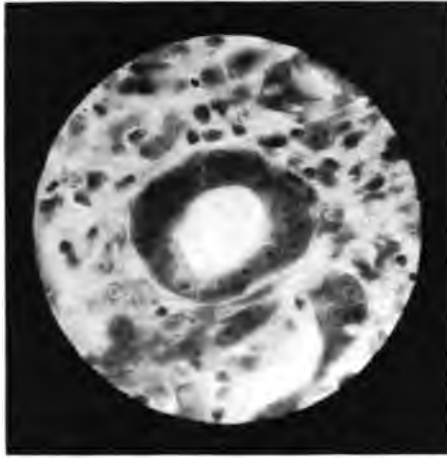


Fig. 84.—(35572) Photograph of undifferentiated, irregular epithelial cells in the submucosa, just below the muscularis mucosæ. The cells are typical of carcinoma.

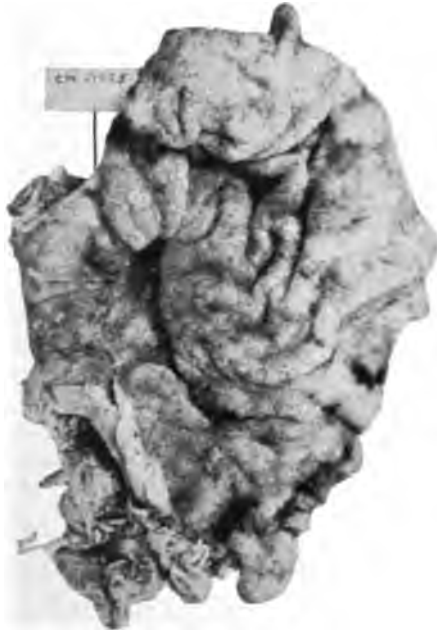


Fig. 85.—(21555) Photograph of chronic gastric ulcer.

noma group, and a doubtful group. Whenever the clinician feels positive of the clinical diagnosis of chronic gastric ulcer, he should



Fig. 86.—(21555) Photograph of chronic gastric ulcer.

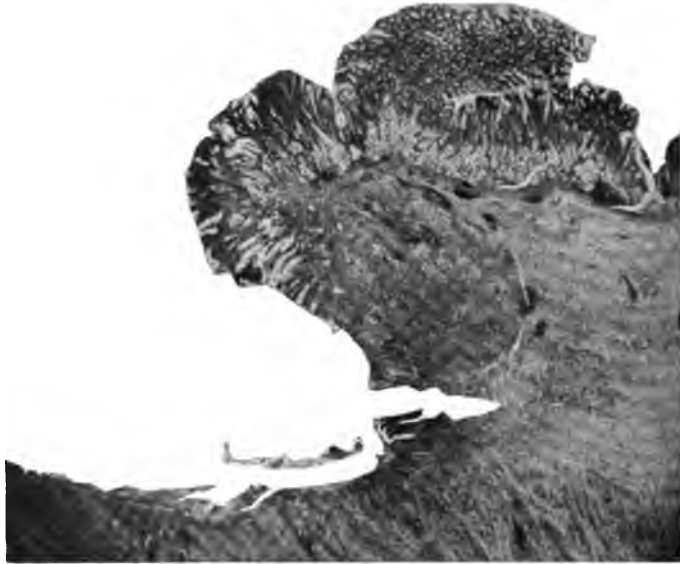


Fig. 87.—(21555) Low-power drawing through the border and part of the base of the ulcer, showing the presence of carcinoma in the mucosa and just below the mucosa, but more in the base. Direct connection between the glands of the mucosa and the carcinoma may be seen.

consider that carcinoma cannot be ruled by our present methods of clinical investigation.





Fig. 88.—(21555) High-power drawing through an epithelial carcinomatous island in the submucosa of the gastric ulcer in Figs. 85 and 86.



Fig. 89.—(21882) Chronic gastric ulcer plus the presence of carcinoma.



Fig. 90.—(21882) Gross section through the carcinomatous ulcer which is seen in Fig. 89

## CARCINOMA OF THE STOMACH \*

CHRISTOPHER GRAHAM

The difficulties that surround the diagnosis of cancer of the stomach and the unsatisfactory results that attend surgical interference continue to hold the disease among those most dreaded.

At present, indeed, the problem of diagnosis is often quite insurmountable. The disease may be so insidious in its onset, so lacking in urgent early symptoms, that the patient is beyond help before pain or other danger-signals have awakened him to his condition. He may present himself with such trifling trouble apparent that even the careful clinician is not aroused to the gravity of the situation and the patient is lightly dismissed only to await the fatal period. He has appeared at the clinic not from any grave fear, but rather because of loss of appetite for a few weeks, loss of flesh, strength, and color, because he is unable to exert himself, or because some friend has urged him to undergo an examination. Another may tell of his failing appetite and strength, of his inability to prosecute his work, and, accidentally finding a tumor, he presents himself for a solution of the trouble. Not one of these comes because of so-called digestive disturbance, yet most of them have a queer, though perhaps mild, gastric distress; but even at this time we find many beyond any reasonable hope of cure.

Often in cases of gall-stone disease and peptic ulcer we find a characteristic group of symptoms that easily and rapidly lead us to a satisfactory conclusion. But when we are confronted with the necessary signs that lead us gravely to consider gastric cancer,

\* Read before the Medical Society of the Missouri Valley at Kansas City, Mo., March 20, 1913. Reprinted from *The Medical Herald*, July, 1913, 238-244.

we do not have that train of definite symptoms upon which we can clearly base a reasonable diagnosis. Therefore, the frequent failure to discover the true condition early can scarcely be placed upon the clinician and certainly not upon the patient, since the manifest symptoms are not severe enough to arouse his apprehension. Modern education along the lines of preventive medicine



Fig. 91.—(Case No. A79178). Extensive involvement of media and pyloric portion, with marked contracture, producing a gourd-like deformity indicating scirrhus carcinoma. Pylorus gaping, as shown by unrestrained exit of stomach-contents. This is shown by the well-filled duodenum. On exploration found to be inoperable cancer, extensive infiltration; stomach fixed.

will do much toward awakening the laity to a realization of the probable gravity of seemingly mild or unimportant symptoms. Inasmuch as so significant a percentage of cases (10 to 14 per cent.) gives a history of mild beginnings, we should be keenly alert to these quiet, indistinct symptoms that may often confront us in the earlier and more opportune stages.

The histories naturally group themselves into three classes:

First, those with a long precancerous history, perhaps years, which is clearly a history of ulcer (40 to 42 per cent.); second, those who in months or years past had gastric symptoms, but who have had some months or years of perfect freedom; third, those whose troubles come as a thief in the night or who have seemed to leap from health to grave disease (58 per cent. less than two years). As histories are more carefully developed we find that group three decreases, while the first and second groups increase correspondingly. When cancer has once found a foothold and symptoms are manifest, the three groups furnish quite the same clinical picture.

The usual dyspeptic symptoms of pain and distress, gas, loss of appetite, etc., are more or less constantly present in cancer of the stomach, but we find the same symptoms in so many general bodily disturbances that to be of value we must follow their relations one to another as regards (*a*) the time and manner of development and onset, their varying degrees and by what changed, increased or decreased; and (*b*) we must consider quite as important, the appearance of the patient as he presents himself with his burden of complaint. It is this correlation of symptoms and the patient's general attitude and appearance that give us the picture which we may say is cancer of the stomach.

*Pain* is a constant symptom. About 86 per cent. (38 to 43 per cent. acute) of the patients complain more or less severely, while 14 per cent. admit feeling but mild distress or no pain. The pain is usually more or less continuous, with exacerbations appearing, in many cases, soon or immediately after food (35 per cent.). About 26 per cent. give a history of food-ease some time during the period of complaint, while in others the increased pain may come irregularly and at unexpected intervals. Gerhardt says that those patients who fear to eat because of pain that later follows rarely have cancer. This no doubt contains a measure of truth, because patients with cancer lose food desire, hence do not eat and therefore less often connect food and pain (a greater per cent. *no* pain in cancer, than in ulcer). Histories show that with ulcer the appetite continues, so that the patients are constrained to eat, then to suffer and complain, and connect the two in their histories. In

cancer intense pain is not the rule, but it may be described as dull, dead, boring, wearing, depressing, or distressing, rather constantly present, but varying from distress to pain.

*Localization* of pain is not often noted; rather is there a diffuse epigastric pain. Nor is localization to pressure often present because only when the peritoneum is attacked and inflammatory processes set up do we get local tenderness. This also holds true



Fig. 92.—(Case No. A79970). Large dilated stomach, steer-horn type, occupying almost transverse position, displaced to the right. Marked obstruction of pylorus as shown by large residue after six hours. Operation: Inoperable carcinoma pyloric end of stomach. Extensive glandular involvement. Anterior gastro-enterostomy.

in non-malignant ulcers of the stomach. As the disease progresses the pain intensifies, bland food or even drink increases it, and the things that once gave relief, such as vomiting, belching, alkalis, and perhaps foods, now give less relief, although vomiting and belching rarely lose their transitory comforting effect.

*Vomiting*, like pain, is an accompaniment of gastric disturbance and is so frequently present in various general bodily disturbances

that considered alone it may be deceiving. In early cancer of the stomach it is quite often absent, and may be present only late or not at all. However, it is a symptom so often present (60 to 70 per cent.) during some stage that its consideration is of significance. Vomiting increases as malignancy creeps on. Usually it is more apt to accompany the pain caused by food intake. Early it is not abundant or may be only a flow of tasteless liquid. As the disease progresses vomiting becomes more copious, more irregular, and less frequent. Relief to some degree—often quite complete—follows emesis, but the relief may be so short that the patient complains of almost constant pain. The vomitus may be rancid, foul, and ill smelling, with mucus and blood intermixed. The condition of the vomitus varies with the degree of destruction and obstruction. Delayed vomiting with blood, poorly macerated food-bits, and undigested portions is much more common in cancer than in other lesions of the stomach.

*Gas* accompanies the indigestion of cancer and is scarcely second to vomiting in diagnostic value. The time of its appearance, its painful effect, and the relief that follows expulsion are closely related to other symptoms.

*Appetite* is lessened rather early (60 per cent.) and is often the first symptom to call attention to the stomach. Later, desire for food may be wholly lost and there may be disgust for food, usually first directed toward meat.

*Weakness*, almost to prostration, which is not wholly accounted for by loss of food intake, may come on. Exercise is a task, anemia creeps on, emaciation is marked, and the skin finally becomes wrinkled, dry, and yellow. When to this are added the dull, strange, depressing pain, the vomiting of poorly digested masses, blood, and débris, the distressing gas with eructations, the constipation, mental depression and languor, the absence of acids and presence of tumor (50 to 60 per cent.; 95 per cent. of all gastric tumors are cancer) and all this with a steadily downward course, we have every reason to diagnosticate cancer of the stomach and that of a hopeless character.

There are few periods of gain in the natural course of cancer of

the stomach. Careful feeding and nursing may give periods of improvement, but these must not be construed as signs of a benign condition.

The history as it is presented with its varying symptoms and their relation to each other and their changes as to time and intensity is the first great factor in diagnosis. We may repeat that,



Fig. 83.—(Case No. A60329.) Cancer of the stomach. Tumor-mass can be seen projecting from lesser curvature into the gas-bubble. Cardiac end of esophagus narrowed to small canal through which bismuth spurted across the gas-bubble. Note bismuth still in esophagus. The tumor mass has produced hour-glass contraction, the upper segment constituting three-fourths, the lower segment one-fourth, of the stomach cavity, with canalization between the two segments.

however carefully one compiles and correlates the symptoms of cancer of the stomach, he thus obtains but half the picture, because the patient, in his attitude, acts, and appearance, quite supplies the other half and we must greatly depend on this factor when in the presence of gastric cancer.

All aids to a diagnosis must be borne in mind and brought into coöperation in a consideration of these cases. Serology has

given us but little aid. Gastrosocopy has not yielded definite results, and chemical tests give at best only an inference in the way of evidence and are, moreover, cumbersome. Therefore, until a pathognomonic symptom or group of correlated symptoms be found or a specific reaction be discovered, or a curative serum developed, we must base our conclusions for diagnosis chiefly on the clinical history, a task often difficult and tedious.

In summing up points bearing on the diagnosis of cancer of the stomach we should not neglect the aid furnished by differential diagnosis. When we find gastric symptoms which suggest carcinoma, we should also take into consideration pernicious anemia, tuberculosis, disease of the kidney, as well as other general disorders whose urgent symptoms often appear to be purely gastric. Local conditions, such as some pelvic disorders and ulcer of the stomach where complications are grave (hour-glass, large areas, perforation, and contraction), are also to be considered. However, these latter conditions are purely operable ones and surgical procedures for their relief should not be delayed.

*Palpation.*—Palpation is one of the important measures, and is in great favor as a means of diagnosis in cancer of the stomach. If the abdominal wall is not thick and the bowels are well emptied, we may palpate a tumor, determine its size, location, extent, and motility, all of which go a long way toward clearing up the question of diagnosis and operability. Free motility is one of the cheering signs of operability, yet, as Federmann suggests, the stomach may be bound down by inflammatory adhesions to other organs so that motility may be poor, but the operable chances still good. In ascertaining the motility of a tumor the manner of breathing should be carefully observed. If, when filling the chest, the patient at the same time retracts the abdominal wall and thus causes the ascent of the diaphragm, the tumor may not move downward; it often may ascend. A lax abdomen with full free inspiration and descent of the diaphragm will show motility at its best. Palpation also gives us knowledge of liver metastasis, supraclavicular glands, and pelvic implantations; so that with all if palpation be neglected, our work is but poorly done.



*Examination of the Stool.*—Boas found that careful examination of the stool for occult blood was of great value in determining the presence or absence of cancer of the stomach. Others following this method verified his observations. Bardachzi gives his experience and quotes statistics of many careful observers, 70 to 80 per cent. of whose cases persistently gave the test for occult blood in the stools. Kemp gives a percentage of 88, which he con-



Fig. 94.—(Case No. A80456.) Marked filling defect of pyloric end of stomach, showing canalization. Pyloric obstruction with large residue. Operation: Inoperable carcinoma of stomach.

siders significant. Zoeppritz believes that persistent blood in the stools and the patient's steady decline are real evidences of cancer. In testing for blood in the stool patients are put on a meat-free diet for two or three days—even beef soups are withheld; a small part of the entire stool is tested and blood is usually found quite regularly. This procedure should not be overlooked as an aid in diagnosis, particularly in questionable cases.

*X-Ray Examination.*—The *x-ray* in conjunction with the opaque bismuth meal is rapidly becoming of value as a means of diagnosis in diseases of the stomach and seems destined to reach an enviable place. It shows the size, shape, location, clearance or motility, and character of peristalsis of the stomach. Filling defects and hour-glass contraction due to cancer are readily shown. In the latter condition canalization between the two segments is often seen. It is especially useful in revealing cancer situated beyond palpation, high up under the left costal arch. Early cancer, especially at the pyloric end, is not as readily determined as cancer higher up.

Max Feurer and other observers, in their attempts to arrive at an early diagnosis of cancer of the stomach by means of various chemical reactions derived from the urine and from gastric juices, conclude that such methods are impracticable, that the findings are inconstant, and that they arise in the presence of other diseases. Feurer concludes that history, physical examination and gastric analysis furnish the diagnostic data. To these he adds the *x-ray* findings as the next most important diagnostic aid.

*Gastric Analysis.*—The analysis of gastric contents as a routine procedure should not be neglected. Considered alone, it does not give positive evidence because it has no pathognomonic significance, but when taken with the clinical history, it may clinch the diagnosis. Occasionally it may furnish the first real evidence.

The presence or absence of free hydrochloric acid does not differentiate between benign and malignant conditions. Acids are many times reduced or absent in general disorders when the vitality is at a low tide, and free acid may be present in a considerable number of cases in the presence of cancer (44 per cent.). However, when present, its average is moderate (16 to 20) as compared with ulcer of the stomach (50 in gastric and 60 in duodenal). Free acid in cancer is absent in 56 per cent. of cases, while the number showing combined holds relatively high (75 to 80 per cent.). Blood in the gastric content is present in about three-fourths of the cases (about 75 per cent.) which closely corresponds to its frequency in stools as determined by many observers. Rem-

nants (52 to 57 per cent.) and bacteria are found in obstructive cases.

If we were to give a brief picture of cancer of the stomach as the patients present themselves it would be as follows: Early loss of appetite. Distress—a strange, depressing sensation the patient does not call “pain”—is felt usually immediately after meals, though traces of it may continue. This distress varies as time



Fig. 95.—(Case No. A80620.) Large, fish-hook stomach, showing marked filling defect on greater curvature in pars media, giving it a bitten-out appearance. Operation: Extensive carcinoma middle of stomach, involving entire circumference. Omentum and transverse mesocolon attached to stomach where it had perforated. Resection of four-fifths of stomach. Anterior gastro-enterostomy.

goes on to become later a pain more or less constant with decided aggravation after taking food. This dull, queer, depressing sensation cultivates the foreboding attitude the patient so often presents. Rapid loss of weight follows loss of appetite and onset of pain, but greater than lessened food intake would indicate. Loss of strength is even more rapid and more marked than loss of weight (due chiefly, no doubt, to cancer poisoning). Vomiting

at first may not be marked, or there may be regurgitation of mouthfuls of water, tasteless or salty. As the disease advances, vomiting increases in amount, is sour, rancid, mixed with food masses of hours or days of retention, all more or less darkened by presence of old blood. In the late stages the vomiting is irregular. Obstruction does not seem always to be necessary for delayed vomiting. Gas is a distressing symptom, is rather constant, is as persistent as pain, and more persistent than vomiting. Anemia is present, but a low hemoglobin is rare. Cachexia appears as soon as subjective symptoms become prominent. Palpation reveals a ridge or tumor, enlarged glands or other metastases in 60 per cent. of the cases. Gastric analysis shows lessened free acid, old blood, food remnants, sarcinæ, and Oppler-Boas bacilli. The stools show a rather constant presence of occult blood. This is the picture that gradually and sometimes rapidly develops from simple beginnings—the beginnings we hope some day clearly to recognize.

*Treatment.*—Treatment exists only—(1) As it prevents; (2) as it decreases suffering; (3) as it definitely prolongs life; and (4) as it cures. There can be no full discussion of the subject of treatment without considering prevention, and as earnest workers in the profession, this should receive our best attention.

Temperance in all things should be observed: (a) Careful selection of food; (b) its proper preparation for the stomach; (c) avoidance of overwork or any overindulgence. It is generally acknowledged that if these hygienic measures be ignored the incidence of ulcer is increased.

Attention should be given to infections outside the stomach, *e. g.*, appendicitis and typhoid fever, as by prevention or proper treatment of these infections the chances of ulcer of the stomach are reduced.

Ulcer of the stomach is the soil of choice for the development of cancer (50 to 70 per cent.). Therefore, on the proper or improper handling of ulcer must depend in a great measure the frequency of cancer development. Here the question naturally arises: Does medical treatment, which includes diet, rest, alkalis, etc., really control the final condition as well as to hold in abeyance

the distressing symptoms; or does surgery offer more, both in the way of relief of symptoms and holding in check the ultimate cancer incidence? This is a question with a difference of opinion, and in justice to our patients calls for careful weighing. We believe it is a problem which is being solved, although slowly.

With the exception of prevention or precancerous treatment there is today but one known treatment with scientific foundation



Fig. 96.—(Case No. A81837.) Marked filling defect, pars media and pars pylorica, involving greater and lesser curvature. Diagnosis: Carcinoma of stomach, medullary type. Operation: Extensive carcinoma involving lower two-thirds of stomach with metastasis.

for cancer of the stomach, and that is surgery. It is true that surgery has its grave limitations, and without doubt late diagnosis is the greatest. This is partly due to the fact—(1) That there are cases without manifest symptoms until the condition is hopeless; (2) that patients do not seek advice even when symptoms are urgent; (3) that the physician who, because of ignorance, sordid gain, or unpardonable pessimism, holds his patient without consultation through the favorable period; (4) that the overcon-

servative surgeon asks for evidence which, when presented, comes too late; (5) and, most serious of all, that the reckless surgeon who without sense, judgment, or humanity, for a fee, for notoriety, or perhaps for experience, and with the slightest or no evident excuse, advises surgery when simple physic only is required. How many of us have not heard the complaint: "I would have presented myself sooner, but was afraid an unnecessary operation would be advised"? Ruthless surgery has done more than its share to create this feeling of distrust and discontent among patients, suffering with this disease, who are in grave need of honest advice.

Recognizing that a late diagnosis entails great surgical limitations, clinicians should increase their vigilance on all sides and ever be ready to consult with the internist or surgeon when service to the patient may be increased thereby. After making the diagnosis we must consider carefully: (1) Contraindications connected with the general physical condition of the patients, and (2) contraindications connected with the local pathology.

Operation gives little hope of even successful completion if—(1) The tumor crowds well into the cardia; (2) if the cardia be obstructed; (3) if the cancer be diffuse or if the stomach be small and shrunken; (4) if there be extensive glandular involvement; (5) if there be involvement of other organs, as the pancreas, liver, or colon; (6) if foci, as to rectal shelf and ovaries, be transplanted (Palmer, Schaeffer), and (7) extreme cachexia must be considered when operability is questioned even in the absence of tumor or dissemination. Cachexia alone is not a bar to operation. Schaeffer rightly says that operations undertaken when complications are great, hasten, rather than stay, death. He also urges that size, extent, and non-motility of tumor do not always exclude successful surgery if organs beyond the stomach are not invaded. However, enough sound cardiac tissue must remain with which to make the anastomosis.

The surgical prognosis in cancer of the stomach is not flattering, but despite the fact that statistics are depressing, surgery offers some hope to the sufferer. Any promise of relief is better than inaction, and the surgeon can promise a reasonable degree of relief

from suffering or at least in many cases a reduction of suffering. In other cases he can go much further and assure the patient of weeks, months, or years of coveted life, and occasionally a permanent cure. There is a prospect of a five-year cure in about 25 per cent. of the cases, of a three-year cure in 41 per cent. (Mayo).

The prolongation of life would seem the greatest gain to be obtained through surgery—a gain of one and one-half to five years is not infrequent, while patients treated medically rarely live over a year *after definite symptoms develop*. The operative mortality in resection is from 9 to 11 per cent. The two factors alone—prolongation of life and relief of distressing symptoms—are sufficient reasons for the adoption of sensible surgical procedures even if we had no cures. But we do have cures.

The present status of carcinoma of the stomach is unsatisfactory both from the internist's and the surgeon's point of view. The internist has no means of treatment at his command except that given through prevention. His service to the patient lies in his ability to diagnose all disorders of the stomach early, and his acuteness in directing his patient wisely to medical treatment or surgery. That which limits his efficiency is felt by every worker in the field, whether internist, surgeon, radiographer, clinician, or pathologist. To none has been revealed a symptom, group of symptoms, a method, a reaction, a chemical or bacteriologic test upon which to base a reasonable diagnosis sufficiently early to enable the surgeon to take up the treatment when a promise of cure would turn the patient's despair to hopefulness.

The surgeon has done but little more than the internist to further diagnosis, though he has the direct aid of vision and touch at operation to assist him in a correlation of facts. His results are discouragingly poor, and he rightfully demands again and again an *earlier diagnosis*.

The effort to obtain more convincing data is renewed, but difficulties are overcome slowly, some of which we cannot hope to conquer until a chemical reaction is discovered which will supply evidence to hasten the time of diagnosis.

Federmann, like many others, clearly emphasizes the fact that

exploration must often be advised before a positive diagnosis can direct procedures. This is deplorable from many viewpoints. It is a humiliation to the clinician who labors for accurate methods; it is a humiliation to the honest surgeon whose only aim is to relieve the sufferer. It is tragic to the patient who without it suffers hopelessly and goes on to his fate. But, most deplorable of all is the fact that this necessity for exploration opens up the way to the untrained, ruthlessly inhuman operator who hopes in this manner to hew his way to fame.

The just demand for early and better diagnosis finds ready response in the heart of every loyal physician, but there is another demand which calls for reform, reform of this unconstrained so-called surgery—dishonest surgery. Let the profession at large and the army of skilled surgeons in particular fall, not upon the neck, but upon the head, of that horde of operators who, without training, without natural ability, and without conscience advise surgery, surgery, surgery with no thought or reason. When this intolerable evil is uprooted and confidence restored among the laity, we shall have made a great step forward toward the early diagnosis and better treatment of cancer of the stomach.

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# A STUDY OF THE VALUE OF THE QUANTITATIVE ESTIMATION OF DISSOLVED ALBUMIN IN GASTRIC EXTRACTS (WOLFF-JUNGHANS' TEST) IN THE DIAGNOSIS OF GASTRIC CANCER \*

FRANK SMITHIES

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Methods for the estimation of the soluble albuminous products of digestion have frequently been devised with the hope that such might prove of practical service in the differential diagnosis of gastric ailments. Of these methods, the well-known procedure advanced by Solomon had for a time the greatest vogue. Esbach's reagent and tubes proved, however, unsatisfactory and inaccurate from a clinical viewpoint. More recently the problem has been approached from the practical quantitative side, and encouraging work recorded.

Wolff and Junghans report a method for estimation of the amount of soluble albumin in gastric extracts which they claim have given excellent clinical information in Ewald's service at the Augusta Hospital, Berlin.

Theoretically, their procedure has the following basis: In the normal aspirated test-meal there are demonstrable relatively large quantities of soluble albumin by means of precipitating reagents. This soluble albumin appears only through the agency of the gastric enzymes. This fact is proved by testing for soluble albumin, a similar test-meal, which has been chymified but not swallowed. In such event only minute quantities of dissolved albumin are present.

Acting on these observed facts, Wolff and Junghans fed similar

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meals to sets of individuals revealing malignant and benign achylia. Their work appeared to show that in the malignant achylia aspirated test-meals were rich in soluble albumin, while in benign achylia very little of the albumin could be demonstrated.

Three suppositions have been advanced to explain this increased volume of dissolved albumin in the malignant achylia. It has been suggested that the excess of albumin is due—(a) To interference with albuminous resorption; (b) to a “cancer milk,” rich in albumin, which exudes from malignant growths, and (c) to a specific, peptid-splitting ferment from the neoplasm, capable of carrying protein digestion as far as the completely soluble albumin stage.

Clinically, the reaction was shown to be positive in 18 of a series of 20 gastric cancers, and negative in 14 of a series of 15 cases of simple achylia in Ewald's service. Recently, Rolph has reported positive tests in all of 7 cases where cancer was previously in the stomach or secondarily involved that viscus. In 8 cases of benign achylia the test proved negative. Rolph states that gastric contents contaminated with blood beyond a dilution of 1:3000 may give the reaction, and cautions against positive interpretation in instances where there is high combined acid present. In such event peptone is usually present. He claims that cancer of the cardia is not so likely to give positive reaction as is cancer in other parts of the stomach.

#### AUTHOR'S STUDY

In the last 3750 patients presenting themselves for test-meal examination of gastric function in the Mayo Clinic there were 747 instances where gastric extracts showed achylia or were associated with conditions likely to be confused with malignancy. These gastric extracts were all tested for soluble albumin by the Wolff-Junghans method. Records were kept of the association of the results of this test with other test-meal and clinical findings. When the tabulations were completed, the diagnoses were entered on the sheets. In 78.4 per cent. of cases it was possible to obtain confirmation of diagnoses by operation.

*Selection of Material and Mode of Procedure.*—The day previous to the examination of his gastric extract the patient was given 1 ounce of castor oil at 4 P. M. This was followed at 6 P. M. by a motor test-meal consisting of mixed food. At 7 P. M. 20 raw, seedless raisins were given. Twelve hours later (7 A. M., the following morning) the patient was fed 60 grams of second-day bread and 200 c.c. of water. This secretory test-meal was removed from fifty to sixty minutes after administering. The specimen secured was thoroughly mixed, filtered through double hydrochloric-acid-washed papers, and tested for dissolved albumin within an hour of its being obtained from the stomach. On account of the fact that, as has been shown in this clinic (Smithies), but 52.2 per cent. of cases of gastric cancer yield gastric extracts revealing absence of free hydrochloric acid, and that in 15.7 per cent. of cases free hydrochloric acid ranges between 20 and 50, we have deemed it advisable to apply the test for soluble albumin not only to achylas, but also to gastric extracts where the free hydrochloric acid was below 20. In a few instances of suspected malignant ulcer we have performed the test upon gastric extracts with higher free hydrochloric acid content. In such we have been fully alive to the possibilities of error, but for the purpose of gaining information and for comparison we have deemed it wise to make the test.

*Procedure.*—Six absolutely clean test-tubes are required for each test. Those of the narrow type and of 20 c.c. capacity answer very well. The tubes are numbered serially from 1 to 6. They receive respectively 1 c.c., 0.5 c.c., 0.25 c.c., 0.1 c.c., 0.05, and 0.025 c.c. of the filtered gastric extract. These amounts are readily measured by means of a 1 c.c. pipet, graduated in  $\frac{1}{10}$  c.c. By means of a 10 c.c. pipet, graduated into  $\frac{1}{10}$  c.c., the volume in each test-tube is next consecutively brought up to 10 c.c. volume with distilled water. This gives from tubes 1 to 6 dilutions of gastric juice varying respectively from 1:10 to 1:400 (viz., 1:10, 1:20, 1:40, 1:100, 1:200, and 1:400). These figures we have termed "units" of precipitable albumin. The tubes are then inverted several times to insure complete mixture of their contents. One c.c. of the reagent to precipitate the albumin in solution is

then carefully layered upon the contents of each tube. The precipitating reagent suggested by Wolff has proved satisfactory with us. It has the following formula:

Phosphotungstic acid (puriss.)	3.0 c.c.
Hydrochloric acid (concentrated)	10.0 c.c.
Alcohol (96 per cent.)	200.0 c.c.
Aq. dest.	q. s. ad 2000.0 c.c.
Mix and keep in a glass or rubber-stoppered flask in a cool place.	

*Manifestation and Interpretation of the Test.*—If there has been dissolved albumin in any of the tubes, the juncture of the Wolff reagent with the diluted gastric extracts is marked by a pearly white zone or "ring." This is better brought out if the tubes are inspected against a black background. (We have used a piece of black cloth, such as photographers employ when focusing cameras.) The tubes should be inspected at once after adding the Wolff solution. Prolonged standing allows cloudy zones to form which render comparative interpretation dubious.

We have interpreted our results after Wolff and Junghans' suggestion. If the white ring of precipitated albumin appears in tubes 1, 2, and 3 (namely, units of albumin from 10 up to 50), and no further manifestations are present in the remaining three tubes, we have called the test negative. If tubes 1, 2, 3, and 4 exhibit rings (units of albumin from 10 to 100), we have considered the reaction doubtful. The presence of white rings in tubes 1, 2, 3, 4, 5, and above (units of albumin ranging from 10 to 200 or 400), we have taken to denote a positive test.

## RESULTS

The gross results of our work are as follows: Of 747 gastric extracts of the class described above, 318, or 42.6 per cent., gave 200 to 400 units of precipitable albumin; 112, or 15.7 per cent., exhibited 100 units, and 317, or 42.4 per cent., showed less than 100 units. In this grouping 71.5 per cent. of the gastric extracts were from cases showing some degree of gastric retention.

*Consideration of Cases of Cancer.*—There were 215 cases of operatively and pathologically demonstrated gastric carcinomas in this series. In 141, or 65.1 per cent., units of precipitable albumin

ranged from 200 to 400. In 29 instances, or 13.4 per cent., there were 100 units of albumin shown. Combining the returns, it is evident that 170, or 78.5 per cent., of the proved cases of gastric cancer gave either undoubtedly positive or suspiciously positive Wolff-Junghans test. In 45 cases, or 21 per cent., the test was negative, less than 100 units of precipitable albumin being demonstrated. Of this group of 215 cases of gastric cancer, 73.2 per cent. exhibited some grade of motor stagnation.

Gastric extracts from 15 cases of *ulcus carcinomatosum* were tested. In 11 instances, or 73.3 per cent., units of precipitable albumin ranged between 200 to 400. In 3, or 20 per cent., 100 units were shown. In other words, of the 15 cases of malignant gastric ulcer, 14, or 93.3 per cent., were either definitely positive or suspiciously so to the Wolff-Junghans test. One case (6.6 per cent.) exhibited below 100 units of albumin. In this group motor stagnation of some degree was present in 86.6 per cent.

Combining the results from the cases of frank gastric carcinoma and those of *ulcus carcinomatosum*, it is seen that of a total of 230 cases, 184, or 80 per cent., returned positive or suspicious Wolff-Junghans test.

*Relation of Manifestations of Test to Location of Malignant Process.*—We examined gastric extracts from 10 cases of cancer involving the *cardia*. Six cases (60 per cent.) gave positive test, 1 (10 per cent.) was suspicious, and 3, or 30 per cent., were negative. Thus 70 per cent. of our cases of cancer at the *cardia* showed units of precipitable albumin ranging from 100 to 400.

There were 5 cases of cancer of the *fundus* in our series. One (20 per cent.) was positive, one (20 per cent.) was doubtful, and 3 (60 per cent.) were negative.

We have records of 44 cases where the neoplasm involved mainly the *lesser curvature* of the stomach. Of this group, 33 cases (75 per cent.) gave clearly positive Wolff-Junghans test, 4 (9.1 per cent.) were suspicious, and 7 (15.8 per cent.) were negative. It is evident that 84.1 per cent. of cancers involving the *lesser curvature* show units of precipitable albumin ranging from 100 upward.

In our series there were 3 cases of cancer of the *greater curvature*.

Two cases (66.6 per cent.) were positive and the remaining case suspicious. Thus, all showed 100 plus units of albumin.

Eight of our cases were proved to have cancer involving mainly the *posterior wall* of the stomach. Of this group, but 3 cases (37.5 per cent.) were positive to the test, while 5 cases (62.5 per cent.) were negative.

The *pars media* was involved 14 times. Of this number, 11 cases (78.5 per cent.) gave positive test and 3 cases (21.5 per cent.) were negative.

In 93 instances the malignant growth was at the *pylorus* and *antrum*. In this class 59 cases (63.4 per cent.) showed units of precipitable albumin from 200 upward, 8 cases (8.6 per cent.) were suspicious, revealing 100 units, and 25 cases (26.9 per cent.) were negative. In other words, 72 per cent. of the cancers at the pyloric region gave positive or suspicious Wolff-Junghans test.

Our series includes 38 cases where the stomach showed *general* or *very extensive* malignant involvement. In 26 instances (68.5 per cent.) the test was positive, in 3 cases (7.9 per cent.) it was suspicious, while 9 times (23.6 per cent.) negative results were obtained.

*Comparison of Other Test-meal Findings in the Cases of Cancer with the Wolff-Junghans Test.*—It might be profitable here to emphasize the diagnostic relation of other tests associated with that for dissolved albumin in the gastric extracts from our malignant cases. It will be noted above that of the 230 cancer and malignant ulcer cases, the Wolff-Junghans test was positive or suspicious in 184, or 80 per cent. In this same group of cases free hydrochloric acid was absent in 52.2 per cent., lactic acid was demonstrated in 48.8 per cent., "occult" or altered blood shown in 75 per cent., glycyltryptophan test present in 40 per cent. (141 cases), the average formol index (method of Sorenson and Schiff) was 21 (57 cases), and organisms of the Boas-Oppler group were demonstrated in 93.8 per cent. (146 cases) by the colored-agar method (Smithies). Some degree of gastric retention was shown in nearly 74 per cent. of the entire group of cases of cancer, irrespective of the location of the growth.

*The Wolff-Junghans Test in Extragastric Cancer, Liver and Gall Tract.*—Our series includes 15 instances of malignancy in this location. In 5 cases (33.3 per cent.) the test was positive, in 3 cases (20 per cent.) it was suspicious, and in 7 cases (46.6 per cent.) it was negative. Thus 8 cases (53.3 per cent.) of extragastric malignancy showed units of albumin from 100 upward. Some degree of motor stagnation was evidenced in 26.6 per cent. of these cases.

The *pancreas* was the seat of malignant processes 3 times. In no instances was a positive Wolff-Junghans test obtained. Motor defect was not noted in any of these cases.

There was 1 case of cancer of the *transverse* colon. It gave negative test. There was normal motility in this case.

*Gastric Syphilis.*—We have tested gastric extracts for dissolved albumin from 5 cases. The reaction was positive in 2 instances (40 per cent.), suspicious in 1 (20 per cent.), and negative in 2 (40 per cent.). In one of the positive cases the specific process in the stomach was associated with multiple and exuberant ulceration. Gastric motility was interfered with in 1 case (20 per cent.) of this group.

*Primary Anemias (Mainly Pernicious).*—Twenty-four cases of achylia in severe anemia comprised this class. In none of them was gastric stagnation present. Twenty-three, or 95.6 per cent., of this group were negative to the Wolff-Junghans test. In but 1 instance (3.3 per cent.) were the units of precipitable albumin above 200.

*Simple Achylia Gastrica.*—We examined gastric extracts from 35 such cases. Gastric stagnation was proved in 4 cases (11.9 per cent.). In 22 instances (63 per cent.) of this type of achylia the test was negative; in 9 instances (25.9 per cent.) suspicious, and positive but 4 times (11.9 per cent.).

*Achlorhydria.*—In addition to the cases of absent free hydrochloric acid mentioned in the above groups there were 212 cases of non-malignant disease showing achlorhydria. Gastric motility was impaired in 22 cases (10.3 per cent.). In this group 136 cases (64.1 per cent.) were Wolff-Junghans negative, 41 cases (19.3 per cent.) were doubtful, and 35 cases (16.5 per cent.) were positive.

*Simple Gastric Ulcer.*—A number of cases of this affection and of duodenal ulcer were studied for purposes of comparison with the malignant cases. Their gastric extracts generally showed low free hydrochloric acid content. We tested extracts from 33 cases of operatively demonstrated gastric ulcer for dissolved albumin. In 16 instances (48.4 per cent.), units of albumin ranged above 200; in 6 instances (18.1 per cent.) the units ran as high as 100, while in 11 cases (30.3 per cent.) units of albumin were below 100. It is thus apparent that 66.5 per cent. of the proved cases of simple gastric ulcer were positive or suspicious to the Wolff-Junghans test. Gastric motility was delayed in 39.4 per cent. of this group.

*Duodenal Ulcer.*—Gastric extracts from 18 cases of duodenal ulcer were tested. In 12 cases (66.6 per cent.) units of albumin ranged above 200; in 2 cases (11 per cent.), at least 100 units were present, while 4 times (22.7 per cent.) less than 100 units were demonstrated. It is thus evident that 78 per cent. of our cases of duodenal ulcer were Wolff-Junghans positive or suspicious. In this group gastric stagnation was present in 55.5 per cent. of the cases.

*Nephritis and Cardiovascular Disease.*—Our series includes 12 cases of cardiorenal affections associated with obscure gastric complaint and anemia. The gastric extracts showed achylia. In 6 instances (50 per cent.) the Wolff-Junghans test was doubtful, while in an equal number it was negative. The doubtful cases were associated with some degree of gastric motor insufficiency.

*Cases Exhibiting Low Gastric Acidity.*—In this group we include 159 instances where gastric acidity ranged from 2 to 70. The average was 18.7. This group furnished what might be regarded as controls on our reactions in other groups, as well as demonstrated what results might be expected from the Wolff-Junghans test in extragastric, malignant, and non-malignant ailments. It should be emphasized that all the patients examined complained of some gastric disturbance. The finding of the low free hydrochloric acid in some instances might have led to suspicions of malignancy by those who hold gastric acidity as a strong index of



such condition. This might have been especially so when we recall that the average age of our patients is above forty years.

Clinically, this group was varied as to diagnosis. Among the affections were: appendicitis, cholecystitis, cholelithiasis, alcoholic gastritis, gastric neuroses, pulmonary tuberculosis, tabes, multiple sclerosis, tuberculous peritonitis, nephrolithiasis, pancreatitis, cirrhosis of the liver, pregnancy, malaria, diabetes, aneurysm of the abdominal aorta, chronic constipation, hemophilia, cancer of the breast, cancer of the lip, etc.

Of this heterogeneous group of cases of low gastric acidity, 40, or 25.1 per cent., were Wolff-Junghans positive, 38, or 23.9 per cent., were doubtful, and 81, or 50.9 per cent., were negative. In other words, of this class nearly 50 per cent. of cases showed units of precipitable albumin from 100 upward. Gastric motility was interfered with in some degree in 25 cases, or 15.7 per cent.

*Relation of the Wolff-Junghans Test to the Presence of Blood in Gastric Extracts.*—We have frequently tested gastric contents that were discolored bright red by traumatic blood, without getting positive Wolff-Junghans tests. Of our entire series of 747 cases herewith detailed, "occult" blood was demonstrated by the benzdin test in 43.2 per cent. Reference to the gross summary of our work above will reveal the fact that we obtained positive tests for precipitable albumin in 42.6 per cent. of the gastric extracts of the entire series, while in 15 per cent. the test was doubtful. There may be more than a curious relationship between these groups of figures.

#### SUMMARY

The work herewith submitted appears to justify the following conclusions:

1. When carefully performed and interpreted, the Wolff-Junghans test for demonstration of dissolved albumin in gastric extracts was positive or suspicious in 80 per cent. of our series of gastric cancer. In this series it was a more constant finding in gastric extracts than were absent free hydrochloric acid, the presence of lactic acid, and the glycytryptophan test. It was rather more constant than tests for occult blood and the demonstration of

gastric motor inefficiency. It was not so consistent in its manifestation as the demonstration of organisms of the Boas-Oppler group or the increase in the formol index.

2. In extragastric malignancy, gastric syphilis, and nephritis the Wolff-Junghans test is inconstant.

3. In the differentiation between malignant and non-malignant achylia the Wolff-Junghans test, when interpreted in connection with other clinical and laboratory data, is of considerable value. Positive reactions are rarely obtained in the achylia of primary anemia, simple achylia gastrica, and simple achlorhydria when such are unassociated with gastric motor inefficiency.

4. Simple gastric and duodenal ulcers, especially when accompanied by pyloric stenosis or gastric atony, may give confusing responses to the Wolff-Junghans test.

5. The presence of blood in gastric extracts may be a factor in the production of certain atypical positive tests.

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## PALLIATIVE OPERATIONS FOR THE RELIEF OF INCURABLE CANCER OF THE STOMACH \*

WILLIAM J. MAYO

As a result of a public campaign against cancer in Germany, the people of that country have obtained a goodly knowledge of the disease and are fully warned of the dangers due to delay in treatment. The average patients with cancer present themselves at an earlier stage of the disease in Germany than they do in America, and a higher percentage are treated there during the curable period, with correspondingly better results.

A campaign of popular education is now in progress in this country, under the auspices of the American Medical Association and the Congress of Clinical Surgeons of North America. The information thus disseminated will be far reaching, and fruitful results in the near future may be confidently expected.

A high percentage of individuals with cancer are incurable when they present themselves for examination, and only in a certain number of these is a palliative operation indicated. An unfortunate aspect of palliative operation is the effect it has on the patient's relatives and friends. Their knowledge consists of the fact that an operation has been done and that, after more or less suffering, the patient dies. Naturally, they associate the lamentable result with the operation, even though the surgeon has explained to them that an operation would not cure the patient, and the most to be expected for it would be temporary relief. Instances of this nature influence other patients to delay seeking relief during the curable period. Patients often present themselves for examination who have been conscious of a growth for

\* Reprinted from the St. Paul Medical Journal, June, 1913, pp. 269-273.

months, and when asked why they did not come earlier, reply, "If the condition be cancer, it is hopeless any way," and justify their attitude by citing instances of unsuccessful operations on their friends.

Close questioning as regards a history of cancer in the family when making an examination often instils in the mind of the patient that cancer carries with it a stigma. This means that a large number of patients who are operated on successfully keep the nature of the disease as secret as possible. Even friends and relatives may not know the truth. The unsuccessful operations for cancer, however, are widely known.

It will readily be seen that in performing a palliative operation the surgeon assumes a great responsibility. He must be quite sure that the palliation will be sufficient to repay the patient for the expense, the suffering, and the time spent in the hospital, and he should always take into consideration that in the background is an unenlightened public opinion, to be influenced by success or failure. On the contrary an individual with cancer who dies without being operated on may not have sacrificed himself in vain; friends and relatives will be led to seek help with the first symptoms of the disease.

Palliative operations are indicated for the relief of one or more of several conditions which may develop in the gastro-intestinal tract. The most common of these is obstruction, due to the growth, which brings about starvation and death. In the smaller number pain, ulceration, infection, and hemorrhage are the chief factors in the discomfort of the patient and which require relief.

With a view to ascertaining the exact measure of relief to be obtained by palliative operations in incurable cases of cancer of the gastro-intestinal tract, a review has been made of 1000 cases of cancer of the stomach operated on in our clinic during the years from January 1, 1894, to December 31, 1912. Of this number, 378 were radical operations, 376 were explorations in which an inoperable condition was found that did not indicate palliation, and 246 were palliative operations.

One of the most important facts brought out in this study

was that a correct differentiation could not always be made between malignant and benign ulcerations unless a specimen could be removed for microscopic examination. In many of these cases an adequate specimen of the growth could not be obtained because of the location of the disease; for example, on the posterior wall of an extensively adherent stomach. Moreover, when a specimen is obtained for examination it may give an incorrect version of the pathology because it is taken from a point near the disease, but not actually a part of it. If the specimen prove to be malignant, a positive diagnosis can be made, but if it is not malignant, the converse diagnosis is not necessarily correct.

It may unfortunately happen that a specimen cannot be obtained, and the diagnosis is made on clinical findings only. Here the element of human fallibility enters and mistakes occur. If the diagnosis be indeterminate, the patient should have the benefit of the doubt and the condition treated as though it were benign. Gastro-enterostomy was performed for supposed cancer on one patient in our series who is alive and well more than five years. Obstruction existed in this case, and if gastro-enterostomy had not been done, the patient would have died. We have observed other similar cases. It may be taken for granted that those patients on whom a palliative operation was performed for supposed cancer and who lived more than three years did not have cancer.

The inference to be drawn from the foregoing is that palliative operations for cancer of the stomach are not only of value in selected cases in prolonging life and maintaining a comfortable existence, but they are also of value in cases in which the diagnosis is made clinically. The operation gives the patient the benefit of the ever-present doubt as to the correctness of the diagnosis, and a life is sometimes saved which would otherwise be sacrificed. Twenty-two of our patients on whom a palliative operation was performed for clinical or doubtful cancer of the stomach who recovered from the operation and whose after-history was traced lived more than one year. Of this number, 50 per cent. have lived from one to five years; the others are dead, supposedly from malignant disease.

Carcinoma in the vicinity of the cardia producing cardiac obstruction occurs in about 10 per cent. of the cases of gastric cancer. Gastrostomy is a useful means of palliation and should not be delayed to the last resort. Three of our patients on whom gastrostomy was performed lived more than one and one-half years, one lived three years before succumbing to the disease, and during that time was fed entirely through the gastrostomy tube. It happens not infrequently that after using the gastrostomy feeding tube for a time the swelling, from infection and ulceration about the carcinomatous area, will subside, the patient may commence oral feeding, and go on to the termination of life without further use of the feeding tube. A No. 16 English catheter is now being used in our clinic for gastrostomies. The larger tube enables a more varied dietary than the smaller one which was formerly used. The Witzel method of operation is ordinarily performed, but the Stamm-Kader technic is equally effective.

Gastro-enterostomy is an excellent palliative operation in cases of inoperable malignant obstruction of the pylorus, and for those cases with huge excavations in the posterior wall of the stomach which are usually carcinomatous but occasionally benign. If the tumor be large and more or less fixed, as it usually is in inoperable cases, anterior gastro-enterostomy after the Wölfler-Hartmann method gives excellent results and a low mortality. Entero-anastomosis, to prevent vicious circle, has not been found necessary in any of these cases, and so far as could be determined the relief has been quite equal to that obtained in the posterior operation. There is a somewhat higher mortality in the posterior method, due to the fact that greater traumatism is incurred in reaching the posterior wall of the stomach, but the patients have averaged longer life. Of the 10 patients in our series on whom gastro-enterostomy was performed and who lived two years or more, 7 were done posteriorly and 3 anteriorly. Since more were done by the anterior method for malignancy this would apparently be an argument in favor of the posterior operation, but I do not believe it should be so considered. The posterior method is used in the cases of less extensive growths and in the

doubtful cases in which the clinical diagnosis between cancer and ulcer is questionable.

Jejunostomy is a useful procedure, especially in the cases of extensive involvement in which a doubt exists as to whether or not the disease be cancer and in which it is not practicable to remove a satisfactory specimen for microscopic examination. In one case, diagnosed clinically as probable malignant disease of the ulcerative type, the patient was fed three or four months through the jejunostomy tube and recovered. It is now more than two years since the operation and the patient is in excellent health. Jejunostomy is also useful in those cases in which, during exploration, an accident, such as perforation of the ulcer, occurs. These perforations can be wrapped with omentum or the opening can be corked with an omental plug and the patient fed by means of the jejunostomy until healing takes place.

In performing jejunostomy the jejunum is picked up at its origin and drawn out in a loop about 16 inches in length. At this point a nick is made in the intestine and a No. 12 English catheter passed about four inches down the intestine, fastening to the latter with a suture. The intestine is infolded about the tube for one and one-half inches with a suture of silk or linen after the Witzel method, and is then fastened to the margin of the abdominal incision with two sutures. This method is proof against leakage and closes at once when the tube is removed. The attachment of the intestine to the abdominal wall has never given trouble afterward in our cases.

An interesting question arises in connection with palliative operations on the stomach: When it is possible to do so, shall a resection of the stomach be made in cases in which metastases exist beyond the reach of surgical interference? I believe that if the diseased process can be removed from the stomach itself it is wise to operate even if all the glands cannot be removed. It should be remembered that in some instances the glands are the result of an infection and are not malignant. Partial gastrectomy has been performed in our clinic on patients with irremovable lymphatic enlargements who are alive and well more than three years.

## OPERATIVE TREATMENT OF CANCER OF THE STOMACH \*

WILLIAM J. MAYO

The surgical treatment of cancer of the stomach compares favorably in results with the treatment of cancer of any other organ in the human body. When it is taken into consideration that nearly one-third of all cancers occur in the stomach and that their early discovery is a necessary factor in the cure of the disease, the necessity for a clear conception of the value of the various signs and symptoms is at once manifest.

With the hope of obtaining some definite information on these important points an investigation was made in our clinic of the histories of a thousand patients submitted to operation for cancer of the stomach. These operations were performed between January 1, 1894, and December 31, 1912. For purposes of study they have been classified as follows: resections, 378; palliative operations, 246; explorations, 376.

The diagnosis of cancer of the stomach cannot often be made early enough to obtain a radical cure by operation, but a diagnosis of some condition of a surgical nature, probably cancer, can be made in time to permit operative interference in more than one-third of all cases (378 out of 1000). The early diagnosis does not depend on any sign or symptom due to the cancer itself, but on the mechanical conditions produced by the growth. Therefore, in cases of suspected cancer of the stomach the recognition of such mechanical conditions should be the first aim of the diagnostician.

\* Read in the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, at the Sixty-fourth Annual Session, held at Minneapolis, June, 1913. Reprinted from the Jour. Amer. Med. Assoc., August 23, 1913, lxi, pp. 540-548.



A probable diagnosis can be established by simple methods. In 67 per cent. of the total number of cases in this series tumors, some of which were of considerable size, could be palpated. The idea prevalent in the past that finding a tumor indicated an inoperable condition has been proved a mistaken assumption. A movable tumor is a favorable condition, especially if accompanied by early obstruction. We have a number of cases on record of patients who were operated on after a tumor was discovered, who are alive and well after a number of years.

Food remnants in definite amounts were found in 53.3 per cent. of the series, and gross obstruction was present in 20 per cent. Since more than 50 per cent. of all patients with cancer of the stomach have food remnants, it will readily be seen that, next to tumors, food remnants are the most important sign, not necessarily of cancer of the stomach, but of mechanical obstruction. A combination of tumor and obstruction is nearly pathognomonic of cancer in every case otherwise suspicious, and these two easily obtainable signs are of the first importance. Tumors, if present, are usually palpable and obstructive. At least 75 per cent. of cancers of the stomach have their origin in the pyloric end, a situation in which diagnostic conditions develop early. In this connection loss of weight is an important sign; the average loss in this series was 30 pounds.

Cancers of the body and fundus of the stomach occur in about 25 per cent. of all cases. When located at the cardia, these growths produce early obstruction, but are not as yet surgically removable. In the body of the stomach but few can be diagnosed sufficiently early to permit operation, because they are situated behind the margins of the ribs, where a tumor cannot be palpated until a late stage, and, because of the wide gastric lumen, obstruction is a late development. In the few cases we have been able to diagnose early enough to warrant operation the patients were thin and gastropnoxis was present, which made a tumor palpable.

The evidence furnished by the Roentgen-ray is next in importance to the discovery of tumor and food remnants. It is a valuable aid in the diagnosis, not because it demonstrates in the early stage

that cancer is present, but because it shows deformities and muscular deficiencies that are evidences of cancer. It is also of great importance as a means of eliminating from the operative group those advanced tumors of the body and fundus of the stomach which

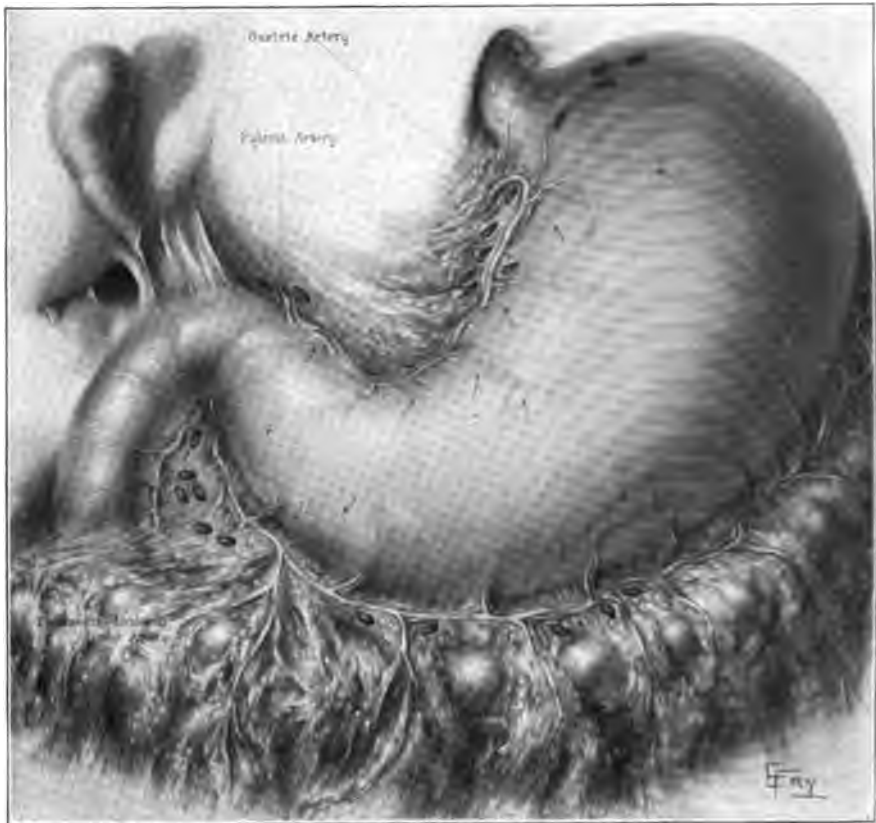


Fig. 97.—Distribution of the lymph-vessels of the stomach.

lie concealed under the ribs, and which have already progressed beyond the reach of surgical aid. The Roentgen-ray also gives valuable confirmatory evidence as regards the presence of obstruction and tumor in cases of cancer of the pyloric end of the stomach.

The examination of the contents of the stomach during the

curable period of the disease is of relative value, but is not pathognomonic.

For purposes of comparison, an investigation has been made in our clinic of a thousand cases of ulcer of the stomach and duodenum in which operation has been performed within the last six years (from January 1, 1907, to December 31, 1912). There was an average total acidity in these cases of above 63, more than five-sixths of which was free. In the 1000 cases of cancer of the stomach there was an average total acidity of 31, about one-third of which was free. These data bear out the accepted hypothesis that low acidity and especially low free hydrochloric acid content is indicative of cancer of the stomach. Low acidity, however, may be found in a large variety of conditions, but one fact was noted particularly, that is, a cancerous stomach always contained some acid, although the free hydrochloric was often absent. The more advanced the case, the lower the acidity and the less the free acid content. Lactic acid was found in 43 per cent.

Blood in some form was found in 73 per cent. of the cases. Severe hemorrhage from the mouth occurred in 4 per cent., coffee-ground vomit in 6.25 per cent., and hemorrhage from the bowel in 9 per cent. Occult blood in the stool was the rule. Occult blood is present, however, in so many conditions other than cancer of the stomach that its value as a positive sign is not great. Smithies states that the Oppler-Boas bacillus was demonstrated in 93.8 per cent. of the last 146 cases of gastric cancer observed in our clinic. These figures were obtained by oil immersion of smears stained by the colored agar method (Smithies).

The gastroscope has not yet been perfected for practical use, although a great deal of experimental work has been done with the instrument (Jackson, Plummer, Janeway, and others) which promises well for the future.

A history of gastric disturbance precedes cancer in a large number, if not the majority, of cases. The average duration of symptoms in the series of 1000 cases was more than two years. This would indicate that in at least the majority of cases of cancer of the stomach some lesion, ulcerous or otherwise, existed

previous to the development of cancer—a point which has been disputed so far as cancer of the stomach is concerned, although accepted for all cancers on the surface of the body, where, so far as we know, cancer has never developed without a previous lesion.

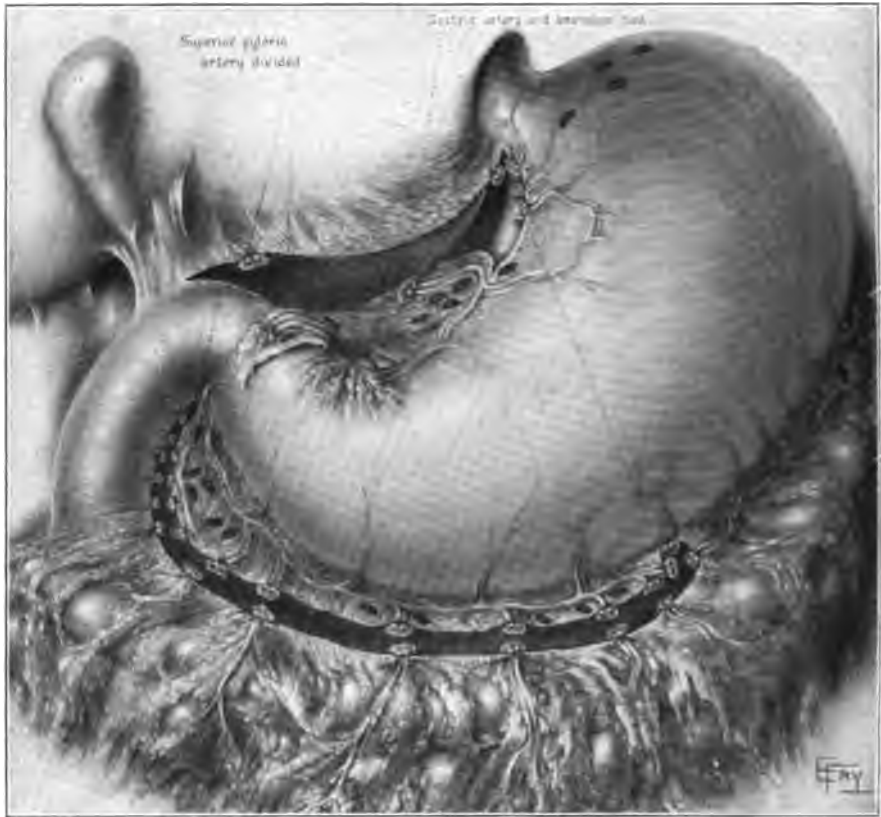


Fig. 98.—Cancer of the lesser curvature of the pyloric end of the stomach, with separation of the lymphatic groups. Dotted lines show proposed resection.

In an investigation by Wilson and MacCarty of 218 cancers of the stomach removed by operation in our clinic, it was found that ulcer or some primary lesion of a similar character had existed in more than 50 per cent.

The art of the diagnostician lies in weighing the evidence at hand, and it is the rule that a correct diagnosis, if made at all, will be made on comparatively few signs and symptoms of definite value. The presence of tumor and obstruction, supplemented by roentgenoscopy and the examination of the contents of the stomach, indicates the lines of investigation. The exploratory incision is the final test, and on the diagnostician devolves the difficult task of determining which of the patients shall submit to such procedures. To give the patient a fair chance exploration must be done early.

Under present conditions the patient who is submitted to exploration with a probable diagnosis of cancer of the stomach has a little more than one chance in three of a radical operation, a little less than one chance in three of a palliative operation, and about one chance in three that the operation will be merely an exploration.

Every operation for cancer of the stomach should begin as an exploration. Exploratory operations for cancer of the stomach are not devoid of danger to the patient. In the 376 explorations in our series of 1000 in which nothing further was done, there were 6 (1.6 per cent.) deaths. In none of these cases, however, could the exploration be considered the direct cause of death. In most of the fatalities the disease was far advanced, a fact that we had failed to estimate correctly.

In cases of suspected cancer of the stomach it is the practice in our clinic to make a small incision in the epigastric midline, opening the peritoneum to the left of the suspensory ligament of the liver. The stomach and accessible portions of the liver are examined with two fingers. In a certain percentage of cases the hopeless nature of the condition will immediately be seen and the wound can be closed at once with buried sutures of linen or silk. This enables the patient soon to return to his family and friends. An exploration of this nature can be conducted under local anesthesia with novocain and the patient disturbed but little. In a large number of cases, however, such explorations are inadequate and the incision must be enlarged sufficiently to introduce the hand in order to make a more careful survey of the stomach, omenta,

liver, and peritoneal cavity. In such explorations the traction on the wound will ordinarily cause enough pain to make the use of ether advisable.

If, on exploration, a resection is deemed possible, the portion



Fig. 99.—Method of closure of the ends of stomach and duodenum by continuous chromic catgut suture, to be followed by musculo-peritoneal suture of linen (see small diagram).

of the stomach containing the tumor is withdrawn from the abdominal cavity for further inspection. This examination will include the transverse colon and mesocolon. Occasionally the transverse mesocolon is involved in the arcade between the main

branches of the middle colic vessels, and the portion involved can be removed without endangering the vascular integrity of the transverse colon. In a few instances in cases otherwise favorable for operation the transverse colon was also involved, and we then resected the diseased portion of the stomach with the involved transverse colon attached. One question rather difficult to decide is, what action to take when the disease in the stomach is mechanically removable, but infected lymph-nodes exist which are not removable. If such patients are in fair condition and the operation can be done without too great risk, we perform a resection. The resulting one or two years of comfortable existence for the patient seems to justify the action.

Moderate involvement of the pancreas does not necessarily preclude operation. Involvement of the pancreas has been considered a bar to resection of the stomach, but we have satisfactorily removed superficial portions of the pancreas in more than 8 per cent. of our resections, closing the end of the duodenum with purse-string sutures and implanting it into the excavation in the pancreas (Meyer). Leakage has not occurred from either the pancreas or the duodenum, and altogether the technic has been most satisfactory. In our earlier work we were much concerned over the possible outcome of these procedures, since Haberkant and Mikulicz had shown a mortality of 70 per cent. or more in like cases. In reviewing our cases, however, we have not found that the mortality was increased more than 1 per cent. as a result of these complications.

Enlarged lymph-nodes will be found in a high percentage of cases of cancer of the stomach, but are not always malignant. The relative degree of involvement may be noted as follows (MacCarty and Blackford): (1) The group along the lesser curvature; (2) the inferior pyloric group; (3) the group along the greater curvature, and (4) the superior pyloric group. Early ligation of the four blood-vessels acts as a starting-point for the separation of the lymph-nodes.

With some exceptions the restoration of the gastro-intestinal tract can be best effected by the Billroth No. 2 method, that is,

complete closure of the ends of the duodenum and stomach with an independent gastro-enterostomy, preferably by the posterior route. If the remaining pouch of the stomach be small, however, anterior gastro-enterostomy appears to answer the purpose equally well and is easier of performance.

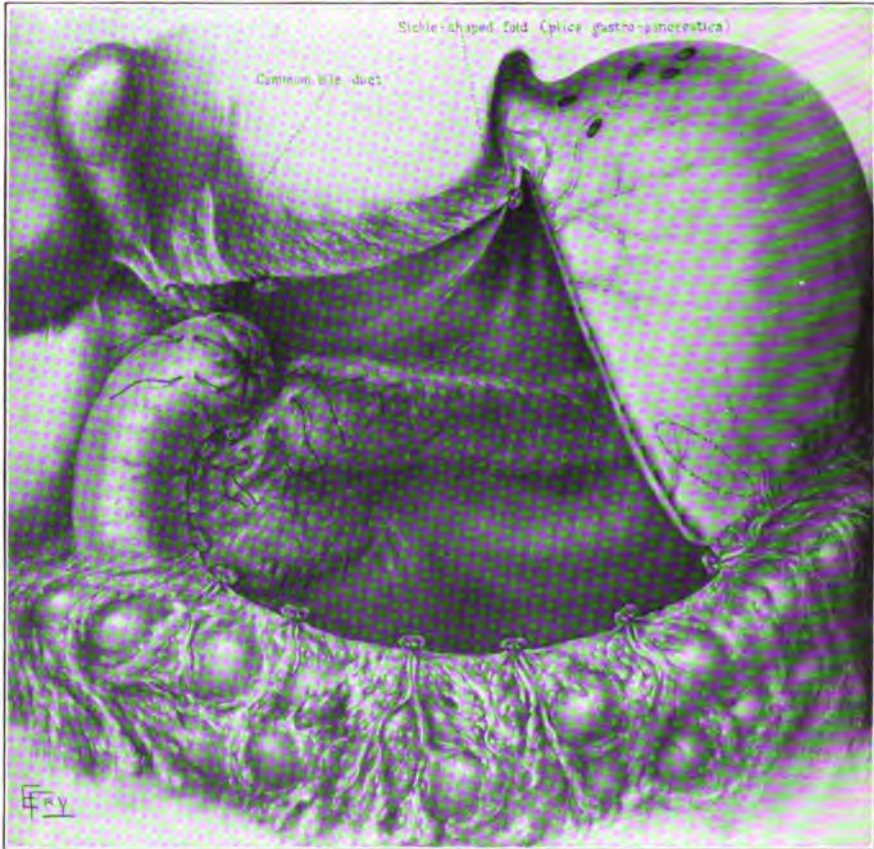


Fig. 100.—Interrupted sutures tying stump of duodenum to pancreas. Dotted lines show posterior gastro-enterostomy.

In some cases of extreme malnutrition it may be advisable to do a gastro-enterostomy, to be followed by a resection in two or three weeks, when the patient is in better condition. We have practised this method occasionally, but, if the case is otherwise



favorable, we prefer to make an immediate resection because it disposes of a foul, sloughing mass in the stomach, and the risk in doing the complete primary operation is little, if any, greater than in doing the operation in two stages. Palliative operations on the stomach are of some value, but they should not be performed except for the relief of mechanical conditions, such as obstruction or, occasionally, when a differential diagnosis between ulcer and cancer cannot be established. In an occasional case perforation of an ulcer with adequate peritoneal protection occurs, but whether it is benign or malignant cannot be determined. If malignant, it cannot be removed, and the operation will be palliative; if benign, a cure results.

Gastrostomy is often a valuable operation in cancer obstructing the cardiac end of the stomach. It should be made with a No. 16 English catheter and preferably by the Witzel method. We performed this operation in a number of instances with a small catheter, about No. 8 or No. 9 English, fearing leakage, but we have gradually acquired confidence in the use of the larger size, which permits greater range of dietary. Pearce Gould has called especial attention to the value of a No. 18 English catheter in gastrostomy.

In pyloric obstruction an anterior gastro-enterostomy after the method of Wölfler and Hartmann is the operation of choice, since it can be accomplished with less manipulation than is necessary to reach the posterior wall of the stomach in order to perform the posterior operation. In our experience a vicious circle has not followed this plan, and the average mortality has been a little more than 4 per cent. We have had a somewhat higher mortality following the posterior gastro-enterostomy for malignant disease, evidently due to the increased manipulation.

Jejunostomy is occasionally a valuable method in cases of cancer of the stomach, especially in those high posterior perforations in which a radical operation is not possible. The involvement may be so high on the stomach that a gastro-enterostomy cannot be done on the proximal side, and in some cases it cannot even be determined whether or not the ulcer is benign or malignant. The jejunostomy is usually made from about 12 to 16 inches down from the origin of the jejunum by the Witzel method

and using a No. 12 English catheter. We have had no leakage in these cases, nor has the attachment of the jejunum to the abdominal wall been a cause of later trouble. Jejunostomy, in cases of either ulcer or cancer, affords adequate feeding and gives complete rest to the involved stomach. If the condition be ulcer, the improvement in nutrition is almost as valuable as rest in stimulating the healing process. A rapid gain in weight and strength is the rule in these cases. The operation is also of great value in cases of accidental injury during the exploration of a cancerous stomach in which resection cannot be done.

#### CONCLUSION

It may be said that with our present means of diagnosis, cancer of the pyloric end of the stomach may be recognized sufficiently early to perform the radical operation in at least half the cases. The mortality is about 10 per cent., depending largely on the class of cases accepted for operation. If an early diagnosis has been made and the patient is in good condition, the mortality will be less than 5 per cent. There is a prospect of a five-year cure in about 25 per cent., and of a three-year cure in 38 per cent., in the case of those who recover from the operation. Comparatively few patients who recover following resection fail to get more than one year of relief.

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# THE TREATMENT OF THE CACHEXIA OF MALNUTRITION

BY METAGASTRIC (DUODENOJEJUNAL) ADMINIS-  
TRATION OF ARTIFICIALLY PREPARED END-  
PRODUCTS OF DIGESTION (AROMATIC  
AMINO-ACIDS AND MALTOSE)

## A Preliminary Report\*

FRANK SMITHIES

There appears to be a class of individuals which, clinically, exhibits weakness, languor, pallor, with or without actual anemia, blotchy, muddy skin, anorexia, dyspepsia, often associated with vomiting and prolonged constipation. In these patients the deviation from the normal can be attributed to no actually demonstrable cause, even after the most careful clinical scrutiny. The cachexia in this type of case is often extreme and may progress to the death of the individual. It is usually ascribed vaguely to 'autointoxication' due to constipation, without apparent regard to what may be the initial factor in the production of such constipation. This group of individuals is difficult to successfully treat, whether by surgical procedure for relief from "toxic" substances said to be absorbed from the large bowel, or by purely medicinal or hygienic measures.

On December 18, 1912, there came to the Mayo Clinic an individual like this, in the hope of securing relief from a surgical operation of the "short-circuiting" type.

The patient was a Russian Jewess, aged twenty-six, whose height was 5 feet 1½ inches, and who, fully clothed, weighed 69½ pounds. She had previously had an appendicectomy performed

\* Reprinted from N. Y. Med. Jour., September 27, 1913, pp. 619, 620.

elsewhere, with a second operation for the relief of adhesions, but without relief of constipation, sour dyspepsia, and cramp-like, general abdominal pains. During the year preceding her coming under observation she had lost in weight more than 30 pounds, was extremely weak, and had gradually become bedridden. Hemoglobin was 70 per cent., urine negative, stomach examination showed normal acidity without retention, with moderate visceroptosis, as shown by air inflation of stomach and bowel, and by radiogram.

Perhaps on account of the patient's extreme emaciation, operative interference was not deemed advisable. The patient was referred for medical treatment. In view of the work of Lusk and his associates\* upon animal calorimetry, and especially that work on the metabolism of dogs following the ingestion of amino-acids, it was decided to observe the effects of similar measures in the human. Fortunately, there was at this time a man in the clinic who was about to be operated on for the relief of a "vicious circle" following gastrojejunostomy for duodenal ulcer. From him we were able to obtain gastric extracts of a golden color, which had total acidity of 68, hydrochloric acid 60, and exhibited tryptic and amylolytic activity of more than 10,000 units by the Gross-Fuld and the Wohlgemuth quantitative estimations. More than 650 c.c. of gastric extract were secured from this patient, filtered through fine sterile sand, and several times through double, hydrochloric-acid-washed filter-papers to free from microorganisms, and then preserved in a sterile flask under toluene (Merck). It was our purpose to avail ourselves of the ferment activity of this gastroduodenal juice, in the preparation of end-products of digestion upon which to feed our patient.

It will be recalled that in the digestion of protein by the gastric juice, it is successively converted through the stages of soluble globulin, acid metaprotein, proteose (propeptone), to peptone. Pancreatic ferments further split this derived peptone to polypeptids, which are then broken up into soluble amino-acids, hexone bases, aromatic amino-acids (tyrosin, tryptophane), and ammonium compounds. The pancreatic juice may, of itself, bring about all stages of protein cleavage. Upon carbohydrates, the pancreatic juice acts completely from the stage of soluble starch through to maltose. The villi of the small bowel, and perhaps the duodenum, take up these soluble products, and from them synthesize the tissue and body fluid protein.

\* Lusk and Richie, *Journal of Biological Chemistry*, 1912, xiii, No. 2, pp. 155-183.

We decided to feed our patient on a mixture of split peptone and maltose. In order to make the procedure as physiologic as possible, we ventured to feed her this mixture by a duodenal tube, metagastrically, *e. g.*, where in the process of digestion such ingredients are normally produced and absorbed. To a saturated solution of Witte's peptone (about 5 per cent. by weight) in distilled water was added 1 per cent. by weight of soluble starch (Lintner). To one liter of this mixture were added 25 c.c. of the filtered gastroduodenal extract. This was incubated under toluene at 37° C. for twenty-four hours. A specimen of the mixture acidulated with 3 per cent. acetic acid, and then tested for free tryptophan, gave the typical rose-pink color reaction. The split peptone mixture, tested independently after incubation, had a formol index (method of Sorenson-Schiff) of 259. A duodenal tube was passed upon the patient in the usual manner. Through it, twice daily, were injected in the early progress of the case 100 c.c., and later, increasing amounts up to 1500 c.c. of the split peptone starch solution. No ill effects were observed. The patient was permitted to eat the same sort of diet on which she had been previously subsisting, and was not put to bed. The bowels were relieved by an occasional dose of castor oil.

The results of the treatment outlined were so encouraging as to warrant its continuance. There were a steady gain in weight and strength, an increased mental activity, a clearing up of the blotchy skin, an improvement in hemoglobin, and an amelioration of the distress associated with constipation. At the end of three months the patient weighed 99½ pounds (a gain of 30 pounds), and was engaged, after nearly two years' idleness, in her trade of hair dressing. At the end of four and one-half months she weighed 114½ pounds (a gain of 47 pounds), and was so well physically that she ceased keeping her appointments for treatment, and had established herself in a little business. She was still constipated. Her hemoglobin had risen to 95 per cent., her complexion was rosy, her eyes bright, and her strength so good that a satchel carrying more than 10 pounds was easily carried, as the patient walked between the houses of her customers. Treatment had been discontinued over two months, and the patient remained apparently normal.

The results in this case were so encouraging as to justify further trial with other patients. Digestion of the peptone was later carried on, with trypsin instead of the gastrojejunal juice. To the split peptone solution was added maltose in the proportion

of 5 per cent. by weight. This mixture was given metagastrically. It appeared to act very well and caused no disagreeable effects. We have used the procedure on two other patients, both women, with cachexia of the type above described. The details of the cases are reserved for a future report. The patients have progressed in a very satisfactory manner.

#### CONCLUSIONS

From the results of our work we feel warranted in suggesting this therapeutic procedure to others for the treatment of cachexia, where surgical relief is not available; where non-obstructing vomiting has become more or less pernicious; where stricture of the esophagus or cardia prevents ingestion of sufficient food to support life; where functional estimations show low pancreatic activity; where grave anemia exists, and in the asthenia following extensive surgical operations. Split peptone-maltose solutions are well borne in the stomach, and there may exist cases where their ingestion through the stomach-tubes may prove valuable.

## PATHOLOGIC DATA OBTAINED FROM ULCERS EXCISED FROM THE ANTERIOR WALL OF THE DUODENUM \*

WILLIAM J. MAYO

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Chronic duodenal ulcers usually occur close to the pylorus, and often produce obstruction. When discovered either at operation or autopsy, they were formerly believed to be pyloric in origin and were classified with gastric ulcers. In no other way can we account for the frequency with which chronic duodenal ulcer is now found as contrasted with the statistics of a few years ago. The types without obstruction were evidently overlooked except in the rare instances when perforation or hemorrhage brought about a fatal termination of the malady.

In spite of the low mortality and gratifying results following gastro-enterostomy for chronic duodenal ulcer, there must always remain a prejudice against an operation which is indirect and does not actually remove the focus of disease. If, however, obstruction exists, this prejudice is not well founded. The calloused, contracted ulcers with obstruction are ideal cases for gastro-enterostomy, which leaves the patient permanently cured. A number of patients upon whom we performed gastro-enterostomy over fifteen years ago remain in excellent health.

In performing gastro-enterostomy for the cure of duodenal ulcer the area of the ulcer should be infolded as recommended by Moynihan. The infolding sutures of silk or linen should be applied in a manner to obstruct the entrance to the duodenum and prevent food from entering the ulcerated portion. As a rule, we place an obstructing suture just above the pylorus for this purpose.

\* Reprinted from *Annals of Surgery*, May, 1913, pp. 691-694.

This method of producing obstruction, although temporary, will last long enough to enable healing to take place. An ulcer so treated will recur but rarely; if recurrence does take place, it will be necessary to make the obstruction permanent, either by complete division of the pyloric end of the stomach and turning both sides in—a method developed by von Eiselsberg—or, more easily but less surely, by drawing a piece of fascia obtained from the sheath of the rectus muscle close about the stomach just above the

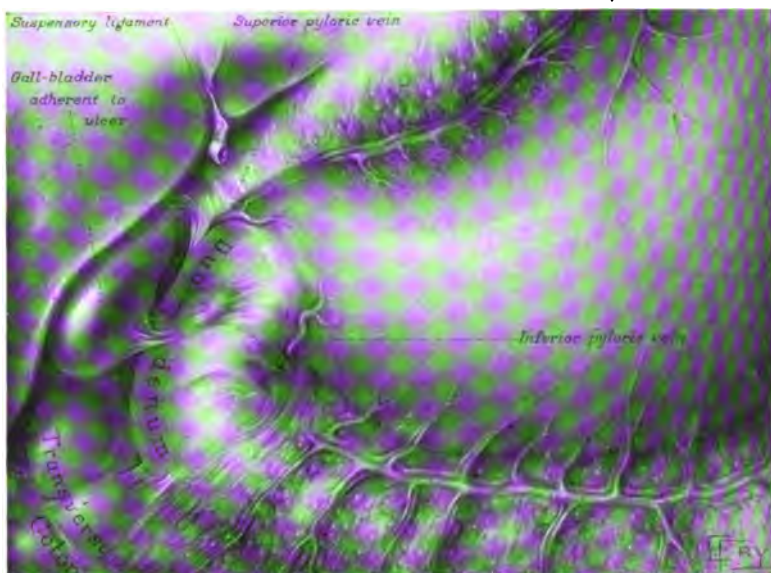


Fig. 101.—Showing external surface of ulcer of anterior wall of the duodenum.

pylorus, and suturing it in such position as to obstruct the lumen, as recommended by Wilms.

Ulcers of the anterior wall of the duodenum may be excised in suitable cases with satisfactory results without performing gastro-enterostomy. The excision of the ulcer should be accompanied by division of the pyloric sphincter, using either the Finney or the Heineke-Mikulicz method of pyloroplasty in the closure. The gastroduodenal opening should be made at least two and one-half inches in length.



We (W. J. and C. H. Mayo) have excised chronic duodenal ulcers in 52 cases in the clinic at St. Mary's Hospital up to December 31, 1912, without performing gastro-enterostomy, and excellent results, both immediate and remote, have followed.

The pathologic examination of these ulcers after excision developed some interesting facts. Basing our expectations upon data concerning ulcers removed from the stomach, we were sur-

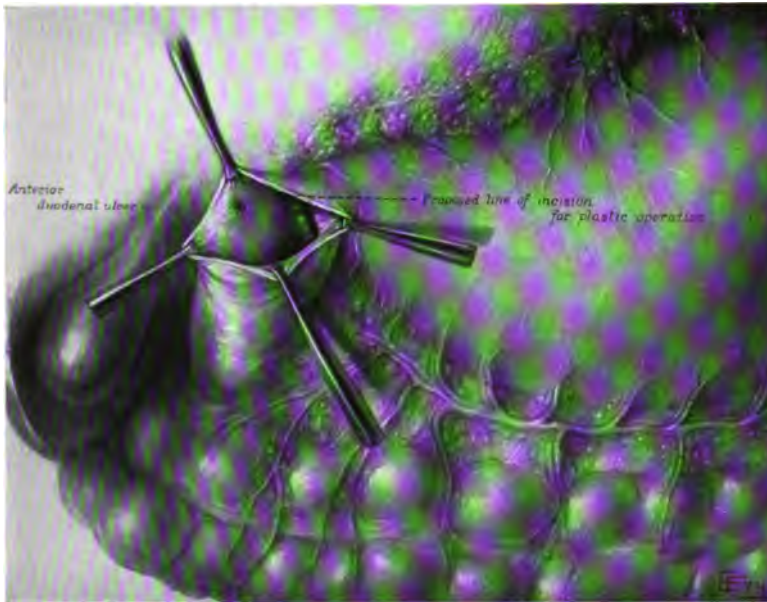


Fig. 102.—Showing mucous surface of ulcer on anterior wall of the duodenum.

prised to find that many of the duodenal ulcers involving the anterior wall had few of the physical characteristics of gastric ulcers. A gastric ulcer is a punched-out defect in the mucous membrane with sclerosed grayish-white base surrounded by thickened margins of somewhat overhanging mucosa. Ulcers on the anterior wall of the duodenum with obstruction and callus upon excision will often show a defect scarcely larger than a dimple. This defect may resemble a little split in the mucosa and is sometimes sur-

rounded by an area of thickened, congested mucous membrane, like a patch set in the duodenum. In several of our cases showing well-marked callus an ulcer could scarcely be detected, but the



Fig. 103.—Plastic operation completed: Finney type.

changed spot of mucosa directly underneath the callus was very prominent. The size of the callus in the submucous, muscular, and peritoneal coats and the amount of obstruction apparently bear little relation to the actual size of the ulcer, which varies from

a minute slit to the size of a pea. Even in the larger ulcers of the anterior wall the base is not often clean-cut and grayish-white, like gastric ulcer, but resembles more a moth-eaten patch. When the peritoneum is involved, the condition of chronic protected perforation develops, with adhesions to the liver, gall-bladder, and omenta. The mucous membrane of the duodenum above the



Fig. 104.—Actual size of ulcer.



Fig. 105.—A photograph and photomicrograph of anterior duodenal ulcer (Case A50019). History of symptoms of eight years.

common duct is smooth, thin, granular, and has few folds. It may be this anatomic peculiarity which prevents the development of thick ulcers of the gastric type. When the ulcer is of the gastric type, that is, a punched-out defect with a calloused base, a raised, corn-like elevation will be found on the peritoneal surface which gives the thickness necessary for the base of the ulcer. In these

latter cases there may be a contact ulcer of the eroded mucous type on the posterior wall.

So far as we have been able to observe, ulcers of the posterior wall of the duodenum present the same characteristics as those of the stomach, that is, a clean-cut, definitely punched-out area,



Fig. 106.—Actual size of ulcer.

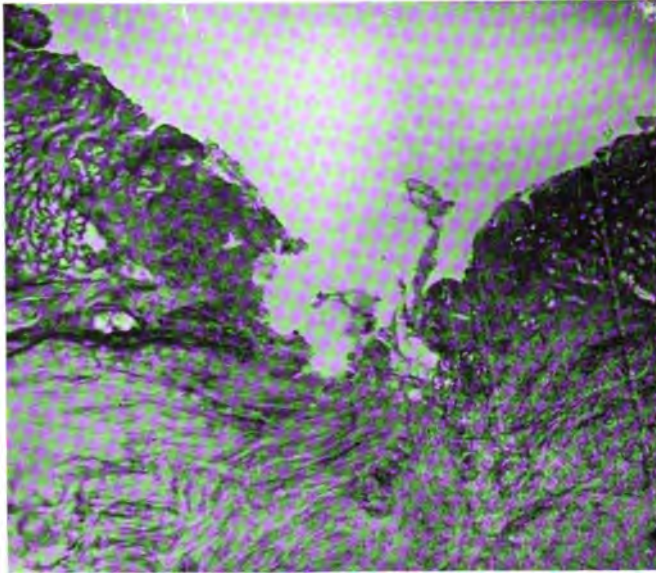


Fig. 107.—A photograph and photomicrograph of anterior duodenal ulcer (Case 49874). History of symptoms for nine years.

attached closely to the pancreas and usually completely perforating the duodenum. They are protected posteriorly by a callus which forms the base of the ulcer. In such cases, however, an anterior contact ulcer will usually be found just opposite the lesion on the posterior wall.

We had excised several ulcers of the anterior duodenal wall before our attention was attracted to the occasional coexistence of an ulcer on the posterior wall by a case in which, after excising an anterior ulcer, a second was discovered posteriorly which had been concealed by the pyloric ring. The ulcer on the anterior wall was evidently secondary and due to contact. In four instances I



Fig. 108.—Actual size of ulcer.



Fig. 109.—A photograph and photomicrograph of anterior duodenal ulcer (Case A75031). History of symptoms for two years: marked obstruction.

excised an ulcer on the posterior wall, suturing the defect from the mucous side. In each case the base of the ulcer was closely attached or fused with the pancreas, and, since it was impossible to get at the posterior wall to apply an outer row of sutures, I contented myself in two cases with a protecting suture at the upper and

lower peritoneal angles. In one case a complete division was made of the duodenum after excision of the ulcer with direct union of the end of the duodenum to the end of the stomach. In the fourth case *devitalizing* mattress sutures were applied from the mucous side in such manner as to cut out the ulcer.

The excision of these four posterior ulcers of the duodenum proved to be so difficult as contrasted with gastro-enterostomy that we are not encouraged to continue the practice, although the patients recovered and remain well. I believe, therefore, that the excision of duodenal ulcers should be limited to those occurring on the anterior wall.

The pathologic findings in these ulcers of the anterior duodenal wall have some illuminating features. They demonstrate just why this type of ulcer might be overlooked and probably is overlooked in the average routine examination of the duodenum at autopsy. The findings also explain why the diagnosis of chronic ulcer of the duodenum may not furnish *x-ray* demonstration. A minute ulcer, unaccompanied by obstruction and without deformity, certainly would not exhibit convincing data. The *x-ray* has, however, been a valuable means of diagnosis in the cases of gastric ulcers and those ulcers of the duodenum accompanied with obstruction—not because of the actual demonstration of the ulcer, but by the determination of deformities and perverted muscular function.

Our limited experience in the excision of duodenal ulcers does not permit us to state that all ulcers of the anterior wall of the duodenum are of the above type, and it may not be true of the thick calloused obstructive duodenal ulcers. As these latter cases are not suitable for excision, pathologic material has not been available. These observations may be of value in drawing attention to the fact that at least a considerable percentage of ulcers of the anterior wall of the duodenum have different characteristics from those of the stomach—characteristics which have been the cause of much confusion because they failed to conform to the standard of gastric ulcer.

## RECURRENCES OF ULCER OF THE DUODENUM FOLLOWING OPERATION \*

WILLIAM J. MAYO

In an investigation of the results following operation on 600 cases of ulcer of the stomach and duodenum in which the history subsequent to the operation was ascertained, Graham found that 86 per cent. were so relieved as to be considered cured, and 11 per cent. were benefited; that is, 97 per cent. were cured, improved, or benefited. The results in the gastric group were not so good as in the duodenal. In the remaining 3 per cent. there was a recurrence of the symptoms following relief of some weeks or months, and several such cases have been reoperated on in our clinic; also a small number in which the primary operation had been done elsewhere were reoperated on here. A study of the findings at the second operation has proved both interesting and suggestive, and it is my purpose to discuss the recurrence of symptoms following operation for *duodenal* ulcer on the basis of this data.

Gastrojejunostomy was the method of choice in the larger number of cases of duodenal ulcers subjected to operation. If actual obstruction existed to the third and fourth degrees, gastrojejunostomy, when properly performed, gave almost certain relief. Plummer points out that such mathematical estimation is much more definite than the use of the terms "marked," "moderate," "considerable," etc., which have only relative meaning, and in estimating degrees of obstruction he advises the use of mathematical equivalents of descriptive terms. For example, obstructions are divided into four groups: (1) Represents those slighter degrees which might or might not be found on different

\* Reprinted from the Boston Medical and Surgical Journal, 1914, clxx, 149-151.

occasions; (2) represents particles of food regularly found later than the normal period; (3) a grade of obstruction which retains certain parts of the food, but allows the bulk of it to pass; (4) retention from mechanical causes which would result in the necessity for removal of such products by the stomach-tube or by vomiting. In response to mechanical obstruction, the stomach acts much like the heart, having periods of dilatation with feeble muscular action in which food remnants are found, and, at other times, good compensation when such remnants are not found. Obstruction to the first degree may be temporary, occasionally taking place as the result of pyloric spasm, which in turn might be caused by any one of a large number of diseases. Obstruction to the first and second degrees, if due to mechanical causes, will ordinarily be relieved by gastrojejunostomy, but not so surely as those accompanied by more marked obstruction as occurs in groups (3) and (4). The greater the obstruction within limits, the better the result of gastrojejunostomy, and, conversely, those cases with slight obstruction or without obstruction have not quite so high a percentage of cures. The difference is less marked, however, than we had been led to expect from *a priori* reasoning, viz., only about 1 per cent.

Failure to cure and recurrences following operation can be divided into two general groups: First, failure of the operation to relieve the stomach of its acid, irritating secretions, and inadequate protection of the ulcer itself during the healing period. This condition occurs more often in those cases without obstruction or with obstruction to the first degree in which gastrojejunostomy has been done, especially the well-nourished individual without obstruction. The pylorus is open and much of the food passes out of the pyloric orifice in preference to the gastrojejunostomy. In such cases attempts have been made to close the pylorus, thus forcing the food out of the gastrojejunostomy opening. Such closure of the pylorus may be brought about most simply by infolding the pyloric end of the stomach with buried silk sutures. Fowler used silver wire for this purpose. Lambotte passes a piece of twine about the stomach just above the pylorus, ties it



tight enough mechanically to obstruct, but without sufficient tension to interfere with, the circulation, which would result in casting the ligature into the lumen of the organ. In radiograms following the bismuth meal Lambotte has shown the pylorus blocked years after such closure. The general experience has been, however, that closure by the use of sutures has not produced a permanent blockage, but that these sutures are eventually passed into the lumen of the stomach, with restoration of the channel, a result which rather regularly takes place in experiments with the normal stomachs of dogs, cats, etc. To obviate this, Wilms introduced the practice of removing a piece of living tissue, *i. e.*, a strip of the sheath of the rectus abdominis muscle one-half inch wide and 4 or 5 inches in length, which was drawn twice around the pyloric end of the stomach, pulled sufficiently tight, and fastened, acting as a living obstruction. This has also been done, using a strip of omentum (Kolb). For some time the method introduced in our clinic by C. H. Mayo has been practised in such cases, that is, cutting a strip from the gastrohepatic or gastrocolic omentum, leaving it attached at one end and drawing it twice about the stomach just above the pylorus, or, if the ulcer of the duodenum is sufficiently far below the pylorus, the omental strip is passed about the duodenum below the pylorus, between it and the ulcer. The site of blocking should be diminished in size by the application of several interrupted sutures of fine silk to take the strain during the healing process. Since we have used this procedure, the blockage remains permanent, so far as we have been able to ascertain. However, sufficient time has not elapsed to show its exact value, but it is undoubtedly true that living tissue drawn about the pylorus is more permanent than mechanical devices in which foreign bodies, such as threads, are used. Recently I reoperated on a case in which the pylorus had been closed in this manner for somewhat more than a year. The strip of living tissue was still in place, and covered with adhesions, and the pylorus was securely blocked. Von Eiselsberg divides the pyloric end of the stomach and closes both ends. This method is sure, but with a definite, although small, mortality. Haberer advocates the unilateral

exclusion of the pylorus (von Eiselsberg) in all ulcers of the pylorus and duodenum, not only because of the certainty of preventing food and gastric secretion from passing into the ulcerated area, but also because it prevents pyloric spasm and traction on the adhesions. In some instances this latter condition is the cause of much pain and distress. While the unilateral exclusion has not been used in our clinic as a primary operation, it has been found very successful as a secondary procedure for the relief of pain, of recurring hemorrhage, or recurrence of the ulcer-syndrome in patients on whom a gastrojejunostomy had been made which was mechanically successful, but in which some of the above symptoms continued. For several years it has been our practice, in duodenal ulcer without obstruction, and in which the conditions were favorable, to remove the ulcer from the duodenum by excision if possible (Mayo, W. J.). In our early cases the ulcer alone was excised. A considerable percentage of the cases subjected to simple excision relapsed within a year, and it then developed that, in addition to the excision, it was necessary to do some type of drainage operation, either gastrojejunostomy, or a plastic on the pylorus, preferably the gastroduodenostomy of Finney. The Finney operation lends itself admirably to excision of ulcers of the duodenum, the ulcer being drawn directly into the operative field as the sutures are placed and can be excised with great ease and safety. Following gastrojejunostomy, if obstruction to the first and second degree exists, the ulcer should be infolded, as suggested by Moynihan, and the pylorus blocked by living tissue, and especially should this be done if no obstruction, potential or actual, exists. If obstruction to the third and fourth degree be present, nothing more than gastrojejunostomy is essential, although infolding the ulcer is advisable. When hemorrhages were noted in the histories of the patients, the blood-vessels were caught by sutures and tied.

In the second group of cases recurrence of the ulcer following gastrojejunostomy was apparent rather than real, and had its origin in improper suturing in the gastro-enterostomy. This happened in some cases which were most favorable for gastrojejunostomy even when obstruction to the third or fourth degree existed

at the time of the primary operation. Secondary operation showed that there was no recurrence of the original ulcer, but that a new ulcer had formed at the site where the gastrojejunostomy was made, due to heavy silk or linen sutures hanging in the gastrojejunostomy suture line. Radiograms following a bismuth meal before reoperation showed that the gastrojejunostomy was not working well and that food was delayed in passing out of the stomach. The acidity of the gastric secretions in these cases was high, and the retention of secretions on an empty stomach, as shown by the stomach-tube, indicated a high degree of hypersecretion, in fact, the whole ulcer-syndrome had redeveloped to such an extent that recurrence of the original ulcer seemed certain.

In a previous paper I have reported cases of gastrojejunal ulcer secondary to gastrojejunostomy due to defects in the operation itself, and especially suture ulceration. Further experience has confirmed the views then expressed. The length of time these sutures will hang in the suture line is remarkable—one case as long as twenty-two months after the original operation. Eight cases of this description, in five of which the original gastrojejunostomy was performed in our clinic, were reoperated on. In two (one of our own) there were intercommunicating fistulas between the stomach, jejunum, and transverse colon. Both of these patients had feculent material in the stomach. The finding of colon contents in the stomach following gastrojejunostomy is an indication of perforating gastrojejunal ulcer into the transverse colon. In a third case an abscess was found connecting a perforation of such an ulcer to the abdominal wall. In five of the cases reoperation showed a heavy strand of silk or linen hanging in the wound, and I have reason to believe that this was the original cause of the gastrojejunal ulcers in the others. In two cases the condition of the tissues were such that after removal of these heavy ulcerating sutures it was thought wise to cut away the gastrojejunostomy, completely restoring the wall of the stomach and jejunum by suture and then doing a plastic operation on the pylorus. This procedure proved so difficult that in later cases the gastrojejunostomy was reopened

in the suture line and the suture extracted. The opening was then enlarged by a plastic operation, using interrupted sutures for the purpose. Experiences of this kind teach that very fine silk, not heavier than 0, should be used for gastrojejunostomy, that the bite of the sutures should be as near the margin of the incision as possible, and that, if it is necessary to reinforce a weak suture line, interrupted fine silk sutures are advisable or such sutures used for part or the whole of the outer row. It has been our practice for a long time to use catgut for the inner row, but it is not the inner row that gives trouble. It is the outer or musculoperitoneal suture, and I have no doubt that if the order were reversed, using silk or linen for the inner row and catgut for the outer, better results would follow. However, catgut is so good a culture-medium that one hesitates to use it on the peritoneal surface of a necessarily infected wound.

If the margins of the opening in the transverse mesocolon contain fatty tissue, it should be sutured to the stomach rather than to the gastrojejunal suture line. Otherwise, it may form a collar-like mass constricting the opening (Mayo, W. J.).

The gastrojejunal opening, as a rule, should be placed directly under the cardiac orifice and not in the pyloric end. The point usually selected is on the lesser curvature, a little to the right of the incisura angularis, and passes vertically oblique to the left. Two cases of contracture of a gastrojejunostomy made in the pyloric end close to the pylorus have occurred in our experience; in neither of the cases was the original operation made in our clinic. There were no symptoms of recurrence of the ulcer in these two cases, but only those of interference with drainage from contraction of the opening, and in each case the gastrojejunostomy was reduced to small size. In both of the above cases the gastrojejunostomy was cut off and made at the usual situation with permanent relief. It is evident that an opening made in the muscular pyloric end of the stomach has a greater tendency to contract than when made at the point of election.

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## CHOLECYSTITIS AND THE FACTORS THAT CONTROL RESULTS OF OPERATION \*

CHARLES H. MAYO

The surgical treatment of diseases of the digestive system is now a common procedure. The symptoms which are directly attributable to the stomach, and those of a reflex character from other causes, so commonly referred to this organ, assume great importance in diagnosing diseases of the abdominal organs. This is especially true of those diseases which are concerned in the digestion and preparation of food for absorption. However, it is often difficult to distinguish true gastric symptoms from those that may be caused by remote conditions in the abdomen as well as those influenced by the general health and the mental status of the patient. Direct observation of the transitional changes caused by disease of the organs concerned in digestion, together with a correlation of facts obtained at autopsy, has added greatly to our knowledge regarding changes in secretion, erosions and ulcers, as well as benign and malignant tumors of the stomach. Undoubtedly within the next few years accurate data will be obtained concerning the disturbances which lead to changes in the acidity, and the conditions which lead to the ulceration, of the stomach and of the duodenum. Even now, in the consideration of digestive disorders, many look upon gall-stones as the source of serious trouble only when colic occurs. Our knowledge of the development of these diseases shows that not only the local infection may cause symptoms, but also that they may be due to secondary obstruction or derangement of the pancreatic secretion, with consequent change in the digestion and delivery of the chyme from the stomach itself.

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Some of the important factors in the production of disease are those infections which derange the alkalinity of the duodenal and pancreatic secretions, especially by infected bile. The acid chyme from the stomach is intermittently emptied into the bowel, a process which Pawlow has shown is accomplished and repeated as neutralization of the acids is completed. Thus conditions of temporary tension in the stomach through so-called pyloric spasm may be produced by derangement of the balance of the alkalinity of the neutralizing secretions. It is well known that pyloric spasm and even regurgitation into the stomach from the upper intestine may occur from interference with peristalsis of the small bowel, as well as from irritation of the appendix.

The liver and its biliary secretion are influenced by the invasion of bacteria into its ducts and into the gall-bladder, and also by obstruction due not only to its own diseases, but to the secondary changes of the pancreas and duodenum, and to adhesions from local infections outside its own tract. Our knowledge of the function of the pancreas, as well as its diseases and influences on digestion when deranged, is slowly increasing. At present we are sure only of the gross changes in these organs. It is still difficult to diagnose clinically, with the abdomen open, between some cases of cancer of the pancreas and a lymphedema from infection and obstruction. Changes in the liver must be gross to be distinguishable. This is but reasonable, since nature has provided such large factors of safety in these great digestive glands that if but a portion be functioning, or if the function of the organ is not too greatly changed, there may be but few recognizable symptoms. Thick mucus in the gall-bladder may occasion considerable colic, while the infection incident to cholecystitis and gall-stones may result temporarily in a greatly reduced acidity of the gastric fluids. In most gall-bladder cases much gas is noted early following the taking of food. This condition is worse in periods, but seldom entirely absent. Moreover, reflex gastric symptoms are nearly constant, but of varying severity, and do not occur in marked attacks or spells, as noted in true ulcerous conditions, although both symptoms may occasionally be found existing in the same individual.

Another important diagnostic point is qualitative food dyspepsia, in which certain kinds of food, especially apples, cabbage, greases, etc., shortly after ingestion, occasion distress, colic, gas, and eructations. This is in contradistinction to quantitative

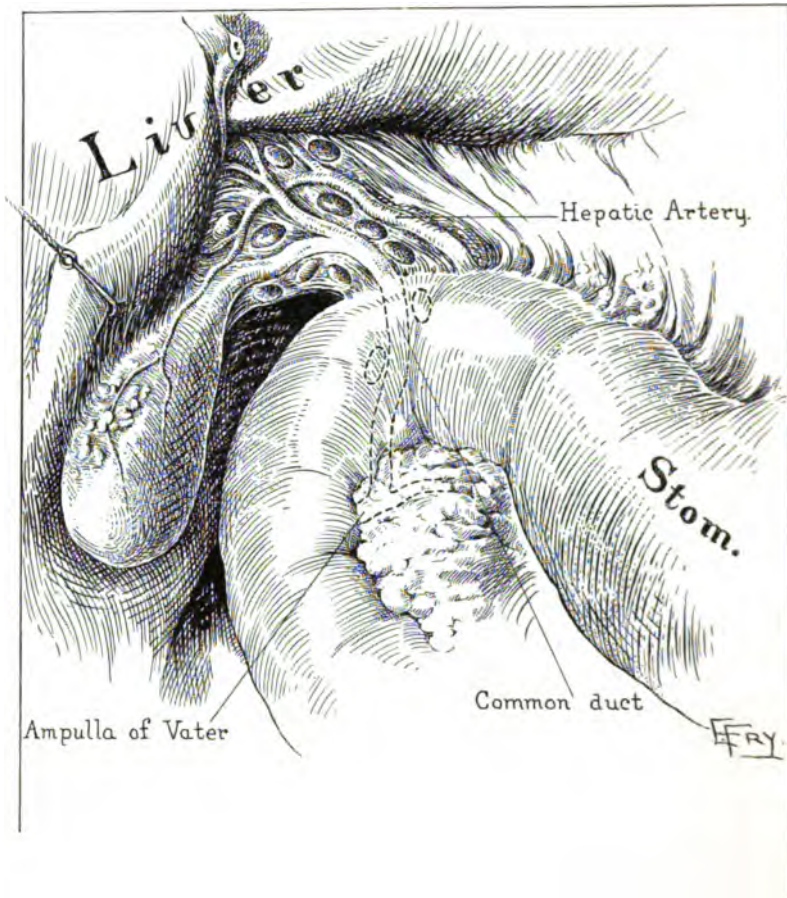


Fig. 110.—Glands draining gall-bladder, head of pancreas, and duodenum.

food distress, averaging two hours after eating, which occurs in cases of intestinal kink and chronic appendicitis with concretions, and which is caused by interference with peristalsis.



It is most necessary carefully to weigh the evidence of the various symptoms, which are believed to be caused from the diseases involving biliary excretion before an operation is undertaken. In many cases it is impossible to differentiate between gall-bladder disease, duodenal ulcer, and appendicitis. Often also more than one disease is present. However, all these conditions are surgical, and exploration is indicated in the majority of cases. Yet the more the symptoms of these serious conditions overlap, the more probable is the foundation purely nervous and the less probable that operation will benefit the patient.

The importance, then, of being able to diagnose cholecystitis when the abdomen is open is of great moment. It is usually easy enough to identify stones and infections of the gall-bladder secondary to obstruction. In cholecystitis, however, serious infection, with foul-smelling bile and "strawberry" mucosa, may not change the normal blue appearance of a thin-walled gall-bladder and may not cause adhesions about it.

In many such a case the abdomen has been closed without the true condition having been recognized. The main object of this paper is to call attention to the means at hand with the abdomen open, which should lead the operator to a correct diagnosis of cholecystitis, and prove the presence of a diseased gall-bladder, or force him to search for disease of some other organ.

I wish to call attention to a group of glands which extend along the common and hepatic ducts, and one or two glands which are located on the cystic duct. These glands can be palpated normally with one's finger through the foramen of Winslow, but they may become quite large through infection, and since they drain the lymph from the duodenum, from the head of the pancreas, and from the gall-bladder, disease of any of these three structures will greatly enlarge them. Any case of cholecystitis with sufficient infection to produce symptoms will necessarily affect these glands. A duodenal ulcer or pancreatitis will do the same, and a blocking of these lymphatics from infection of the gall-bladder may cause a dense interlobular lymphedema of the head of the pancreas associated with it. The pancreas has several sources of blood-supply

and also lymphatic returns, but the head of the pancreas is drained by this group of lymphatics. In the majority of cases, if enlarged glands are found, one or the other of these structures will show dis-



Fig. 111.—Fat-protection of area of gall-bladder.

ease. Only rarely is there exception to this rule, and this occurs when there is a general swelling of the mesenteric glands through malignancy or gross infection. This group of glands may be compared to those of the axilla, since when the axillary glands are en-

larged, we at once examine the arm, the breast, and local area for the source of infection. The surgeon should examine this area of the abdomen at every opportunity, that he may inform himself of the average size of the glands in both normal and diseased conditions.

When a definite source of infection is known, the treatment of mild cases of cholecystitis primarily may be medical, and for the same cases, when found surgically, prolonged drainage should rarely be instituted, rather than the removal of the gall-bladder. The majority of cases are undoubtedly best relieved by cholecystectomy. Drainage alone for cholecystitis usually gives but temporary relief. This is accomplished, when desired, not by inverting the fundus of the gall-bladder, but by attaching it to the peritoneal incision. Drainage ceases after a time by closure of the fistula. When the fundus is inverted, the drainage period is short, the gall-bladder healing first because of its peritoneal covering.

Many patients with cholecystitis, gall-stones, and diseases of the gall-ducts fail to obtain complete relief of symptoms following the primary operation, and a secondary operation often shows adhesions of the pylorus or first portion of the duodenum to the liver, with consequent fixation and angulation. The fatty round ligament with the gastrocolic omentum may be utilized surgically in constructing an apron of fatty tissues, which is attached near the cystic duct and which effectually separates the stomach and duodenum from the liver. Should adhesions occur, the fatty tissue between them permits of extreme pliability.

## CHOLECYSTITIS WITHOUT STONES OR JAUNDICE IN ITS RELATION TO CHRONIC PANCREATITIS \*

WILLIAM J. MAYO

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Cholecystitis without stones is comparatively a common disease, and of late has come into considerable prominence. The types vary in intensity from the mild chronic catarrhal to those characterized by necrosis of the mucous membrane, perforation, and other manifestations of severe bacterial infection.

A certain amount of uncertainty exists as to when chronic cholecystitis should be considered surgically. Not infrequently the condition is associated with appendiceal infections of a chronic character, especially those forms of appendicitis in which foreign bodies, usually fecaliths, are present. Whether or not such appendicular infections are the direct cause of the infections in the gall-bladder has not been determined, but it seems possible, inasmuch as bacterial or toxic products are picked up in the derivatives of the portal circulation, carried to the liver, and there destroyed or excreted in a modified form with the bile. When such infected bile is delayed in the gall-bladder, cholecystitis may result.

The clinical diagnosis of cholecystitis, even when stones are present, is not always easy. With the palm of one's hand an area may be covered which could be involved in pyloric and duodenal ulcer, disease of the gall-bladder, appendicitis, and stones or infections in the right kidney or right ureter. Pain referred to this region may also be due to small ovarian dermoids and early extra-uterine pregnancy. Many times the diagnostician must judge as to the truth of certain alleged facts narrated by the patient, not

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by an examination of the evidence, but by delivering judgment as to the credibility of the statements of the patient. At the time the examination is made there may be no signs which would furnish a basis of differentiation, since the patient is not then suffering from those leading symptoms which he describes.

If these difficulties present themselves when gall-stones are actually present, how much more difficult is it to make a diagnosis of chronic cholecystitis without stones when signs and symptoms are less marked. Even when the abdomen is open, a gall-bladder markedly diseased in its mucous membrane may give little or no evidence of such disease by external examination. In an examination as to the end-results of some 350 patients that had been operated on for gall-stones and cholecystitis, Stanton showed that more than 90 per cent. were cured or satisfactorily improved when gall-stones were present, while in only about 50 per cent. having cholecystitis without stones were the results satisfactory.

Some operators go so far as to say that they never make a diagnosis of gall-stone disease, but tell the patient that he has "an inflamed gall-bladder which needs to be opened and drained." This makes the problem too easy, and leads to "snap-shot" judgment, in which bias and personal equation assume too much importance. If tarry bile, that is, dark-colored bile, containing a considerable admixture of mucus, be accepted as evidence of cholecystitis, a large number of mistakes in diagnosis will not be detected at operation, and a corresponding number of patients will fail to obtain relief, not because of the failure of operation to cure cholecystitis, but because cholecystitis in the surgical sense was not present. This may also be true of adhesions. It should not be forgotten that so-called bands and adhesions are not limited in their development of fetal life, but are continuously forming throughout life. A band of adhesions frequently extends from the gastrohepatic omentum across the duodenum in its second portion, from the gall-bladder to the transverse colon, without causal infection in the duodenum, gall-bladder, or transverse colon, and, of themselves, such adhesions cannot be considered an indication of cholecystitis. In the later period of life there is often a deposit of fat just under-

neath the peritoneum of the gall-bladder, which gives it a whitish appearance and a feeling of thickness to the touch without any infection of the organ itself, but which may be mistaken for evidences of cholecystitis. The most reliable sign of cholecystitis is markedly enlarged glands along the common duct and at the juncture between the common and cystic ducts. In cholecystitis of long standing such lymph-nodes may become calcareous. Two cases of chronic cholecystitis were observed in our clinic in which calcareous lymph-nodes compressed the common duct, producing jaundice. In both instances the patients were cured by the removal of the gall-bladder and the obstructing glands.

Chronic cholecystitis produces two types of gall-bladders: First, the large, blue, distended gall-bladder, which does not empty itself normally under compression. The bile in the gall-bladder is thin and often foul-smelling from colon infection; second, the thick-walled, whitish gall-bladder, which is often adherent and contains bile, usually thick and tarry, with a large admixture of mucus. As a rule, enlarged glands along the common duct will readily be detected in both varieties. Enlargement of the lymphatics may be the only sign in some cases to indicate that the gall-bladder is probably diseased. If the symptomatic evidence that cholecystitis is present is characteristic, it becomes necessary to open the gall-bladder and examine the mucosa before a diagnosis can be definitely established. At times the disease will be limited to one area, which will probably not be detected by merely opening and examining the mucous membrane. In such cases the cause of the symptoms may not be discovered unless the entire gall-bladder is removed and subjected to careful scrutiny.

Assuming the foregoing to be true, it can readily be seen that while cholecystitis without gall-stones exists, until the gall-bladder is opened its existence cannot always be determined. Even after opening the gall-bladder and exposing the mucous membrane the diagnosis of cholecystitis in the surgical sense may remain more or less doubtful until the gall-bladder or some portion of its mucous membrane be subjected to examination by the pathologist. Fortunately, for purposes of diagnosis the strawberry gall-bladder is

one of the more frequent types of cholecystitis, the mucous membrane being covered with yellow specks as though from ulceration and deposit of gall-stone material. As a matter of fact, these little yellow specks are the base of the exposed villi of the mucous membrane which have been stripped of their covering epithelium, and their connective tissue has been stained yellow by bile (MacCarty). The disease is strictly confined to the gall-bladder. Not only is the strawberry gall-bladder easily diagnosed on inspection of the mucous membrane, but as high, if not higher, percentages of cures follow radical operation as follow operations for gall-stone disease, because the common and hepatic ducts, if involved at all, will be involved only in a catarrhal process, and not subjected to the traumatism of possible stones which have descended from the gall-bladder into these ducts.

Taking the strawberry gall-bladder as the type, the more variation from it toward the normal gall-bladder, the less the prospect of cure following operation, because of less certainty in the diagnosis. Our scientific conscience should not be satisfied by asserting, on slender evidence, that cholecystitis exists if a diagnosis of gall-stones has been made and stones have not been found. The wish may be father to the thought, and the condition should not be pronounced cholecystitis without such a diagnosis being verified by the pathologist and a grade of severity established which would make it a surgical disease. We all experience humiliation on failing to verify, at operation, a diagnosis of gall-stone disease or cholecystitis. These failures should be classified and recorded in the hospital statistics as "negative explorations of the gall-bladder."

The milder degree of cholecystitis, when subjected to operation, will not present a high percentage of cures, and under existing conditions should usually be considered medical rather than surgical.

Experience teaches another lesson. While cholecystotomy may be an efficient procedure in gall-stone disease when the gall-bladder is otherwise normal and the ducts are free, in cholecystitis the method is not satisfactory. A gall-bladder which can keep up continuous trouble from infection alone without the mechanic irritation of gall-stones will probably not be cured by simple drain-

age, and cholecystectomy will be the proper procedure to follow. As a matter of fact, cholecystectomy is now largely indicated in gall-stone disease, and it may be said that practically all cases of cholecystitis and the large majority (probably 80 per cent.) of cases of gall-stone disease should be treated by cholecystectomy rather than cholecystostomy.

If so much uncertainty can exist with regard to the gall-bladder and its infections, how much more uncertainty must exist as regards the pancreas and its infections. The sense of sight cannot aid in solving the question, as in the examination of the mucosa of the gall-bladder, and a specimen will probably not be removed for pathologic examination. The diagnosis must be established by the sense of touch, and a certain amount of "intuition" on the part of the diagnostician, which, unfortunately, often plays too large a part in his final judgment. For many years I have made it a practice to examine the entire contents of the abdomen with the gloved hand, whenever it was opened for any purpose and the condition of the patient would permit such manipulation. I have been surprised to find how frequently the pancreas showed enlargement, induration, and nodulation, which would have justified a diagnosis of chronic pancreatitis if some disease of the biliary tract had been the original lesion, but in which there was no symptomatic evidence whatsoever that pancreatic inflammation existed.

In the routine examination of patients in our clinic several hundreds of examinations of the stools have been made, many of them in cases of chronic pancreatitis of this type, to try and ascertain whether or not there were symptoms of pancreatic insufficiency. Such a condition was rarely shown either in cholecystitis or in connection with gall-stone disease. It would seem, therefore, that statistics of the relative frequency of chronic pancreatitis should be accepted with some reserve. Evidence which to one would indicate chronic pancreatitis, to another might not do so. Yet that chronic pancreatitis does exist and that it exists most commonly in connection with infections of the biliary tract is an established fact.



The well-marked cases of chronic interlobular pancreatitis involving the head and often the entire pancreas present conclusive evidence of pancreatitis, just as the strawberry gall-bladder presents conclusive evidence of cholecystitis. Such extreme evidences of chronic pancreatitis are seldom found without infection of the biliary tract, but, in cases less marked, the evidence is often insufficient to establish the diagnosis, especially when neither gall-stones nor jaundice are present.

Robson has shown that in one-third of the cases the common duct passes behind the pancreas, so that even if chronic pancreatitis is present, the common duct is not necessarily compressed, and there may be no jaundice. In such cases, however, an infection from the biliary tract may extend to the pancreas and produce chronic pancreatitis. Whether this occurs more often by mucous continuity through the cystic, common, and pancreatic ducts, or, as Deaver has shown, through the associated lymphatics, cannot always be determined.

Estimating at their full value all these possible sources of exaggeration or error, there still remains a group of cases in which cholecystitis of a chronic type without gall-stones and without jaundice is accompanied by undoubted chronic interlobular pancreatitis. In such cases there is no dilatation of the common duct nor is the gall-bladder distended. That chronic pancreatitis is best treated by drainage of the bile-tract is a lesson so thoroughly taught that even in those cases in which there is no evidence whatsoever of interference with biliary or pancreatic drainage, as shown by jaundice and distention of the common duct and gall-bladder, we still adhere to the practice of draining the gall-bladder without regard to the fact that it is the infection within the gall-bladder which has caused the disease of the pancreas and that this infection will probably not be cured by drainage.

It is the object of this paper to show that in the presence of chronic pancreatitis without jaundice and without evidences of back pressure on the biliary tract, the gall-bladder should be removed if it shows marked evidences of chronic cholecystitis, especially the strawberry type.

In at least a half-dozen cases operated on in our clinic the following sequence has occurred: Cholecystostomy had been done for chronic cholecystitis without stones, and with a complicating chronic pancreatitis. The patient was relieved for some weeks or months and then the symptoms returned. Recognizing the need of more prolonged drainage, the gall-bladder was reopened and drained for a considerable period. There was complete relief as long as drainage of gall-bladder continued, but sooner or later, after the fistula in the gall-bladder healed, the symptoms returned.

These cases are characteristic, and I have no doubt have been observed by many surgeons who have been puzzled to know just what course to pursue. It has been our experience that removal of the gall-bladder relieves the symptoms promptly and permanently cures the patient. Just what the future condition of the pancreas may be one has no means of knowing, but I have found that chronic pancreatitis, the result of gall-stone disease, is usually cured by the removal of the stones and drainage of the biliary tract, and that in the chronic infections of the gall-bladder with secondary involvement of the pancreas, in the absence of interference with biliary drainage, cholecystectomy furnishes a satisfactory symptomatic cure.

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## THE SURGERY OF THE PANCREAS \*

WILLIAM J. MAYO

The deep situation of the pancreas renders it difficult to obtain correct knowledge of its diseases during life. The little knowledge which is obtained is due chiefly to the individual experience of various surgeons and to experimental investigations.

The pancreas is derived from two or three buds from the foregut, and early in fetal life is an intraperitoneal organ. When rotation takes place, the pancreas is turned on its right side, losing its posterior peritoneum, which becomes converted into fibrous tissue. Possibly the diffuse character of fat necrosis, both within and without the peritoneal cavity, from pancreatic perforation, can be accounted for in this way.

The pancreas receives its blood-supply from five or six different sources, the most important of which are the superior pancreaticoduodenal, the inferior pancreaticoduodenal, the inferior pancreatic, and the branches that are derived from the splenic artery as it runs behind the superior border of the body of the pancreas. The lymphatics of the pancreas are not collected in one group, but follow the vascular supply—an important fact in connection with the causation of pancreatitis, as pointed out by Deaver.

The pancreas has no true capsule, but, when irritated, one quickly forms from the peritoneum and those tissues derived from the peritoneum (Fig. 112).

The pancreas is hidden by the liver, duodenum, transverse colon, and especially by the stomach. The two latter organs vary in position to a considerable extent. Access to the pancreas for operative purposes is usually best obtained through the gastrocolic

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omenta, drawing the stomach upward and the transverse colon downward. The pancreas, especially the head, is usually fixed in position, but it may be more or less movable in the body and tail. During routine abdominal operations patients are occasionally seen in whom the pancreatic attachments are so loose that the pancreas as a whole can be drawn outside the abdominal cavity.

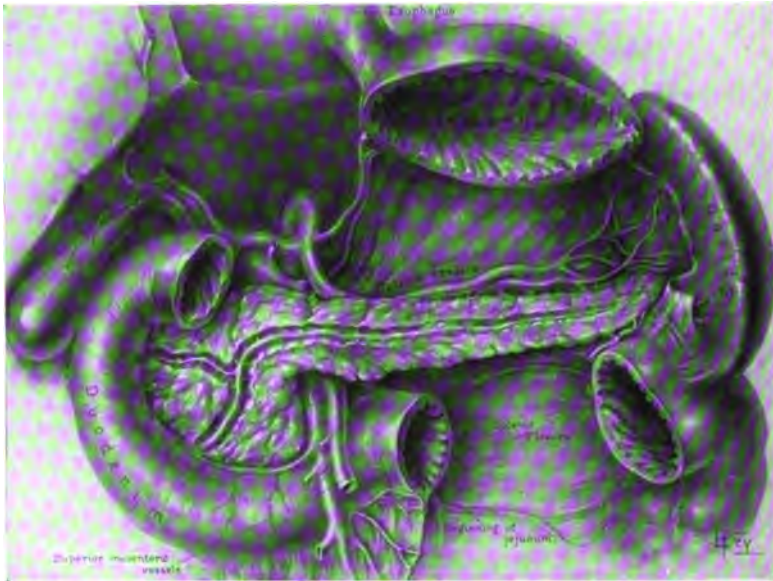


Fig. 112.—Showing anatomy of pancreas and its anatomic relations.

#### I. INJURIES TO THE PANCREAS IN THE COURSE OF OPERATIONS ON THE STOMACH

Haberkant reported a mortality of 76 per cent. in his cases of resection of the stomach for cancer in which there were pancreatic attachments resulting in injuries to the pancreas. Mikulicz found a mortality of 70 per cent. in his cases when the pancreas was injured, as against 27.5 per cent. when it was not injured. In 448 resections of the stomach for benign and malignant diseases up to December 31, 1912 (W. J. and C. H. Mayo), the average

mortality was 10 per cent. In about 8 per cent. of these cases the pancreas was injured and the average mortality was 11 per cent.

In none of these operations, however, was the main pancreatic duct reached—usually only a superficial piece was removed from

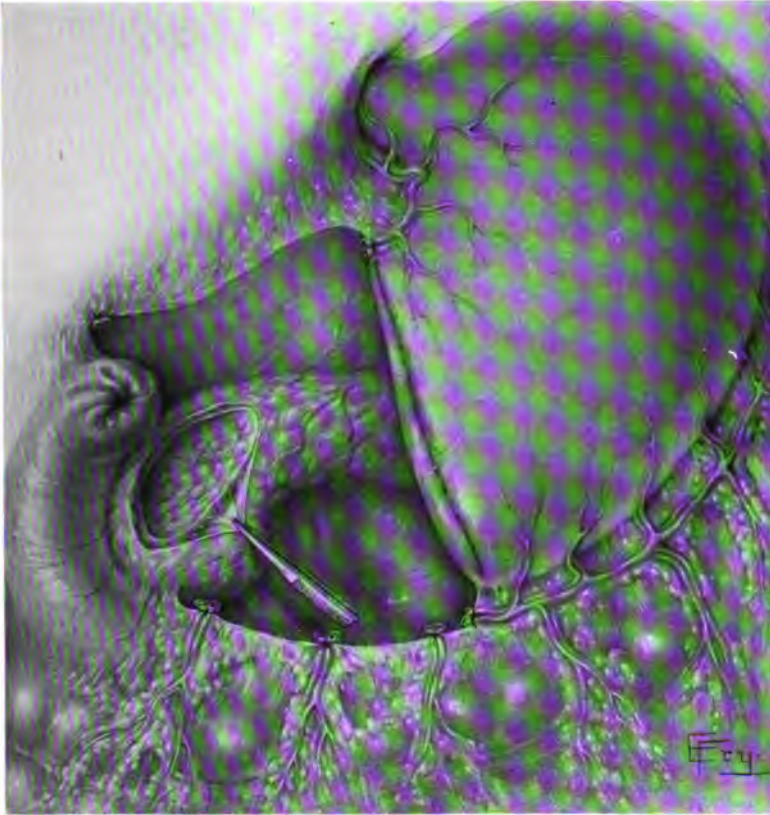


Fig. 113.—Showing excavation in pancreas following resection of pyloric end of stomach with pancreatic involvement. The end of stomach and end of duodenum both closed.

the surface at a point where the pancreas was adherent to the diseased stomach. The bleeding was usually free, and best controlled by catgut on a curved needle. It was noted that in these cases the pancreas had a fibrous capsule, the result of the localized peritonitis.

After removing the pyloric end of the stomach for cancer we close the end of the duodenum with two superimposed purse-string sutures, and then apply the closed duodenal stump directly to the wound in the pancreas, as suggested by Willy Meyer. The an-

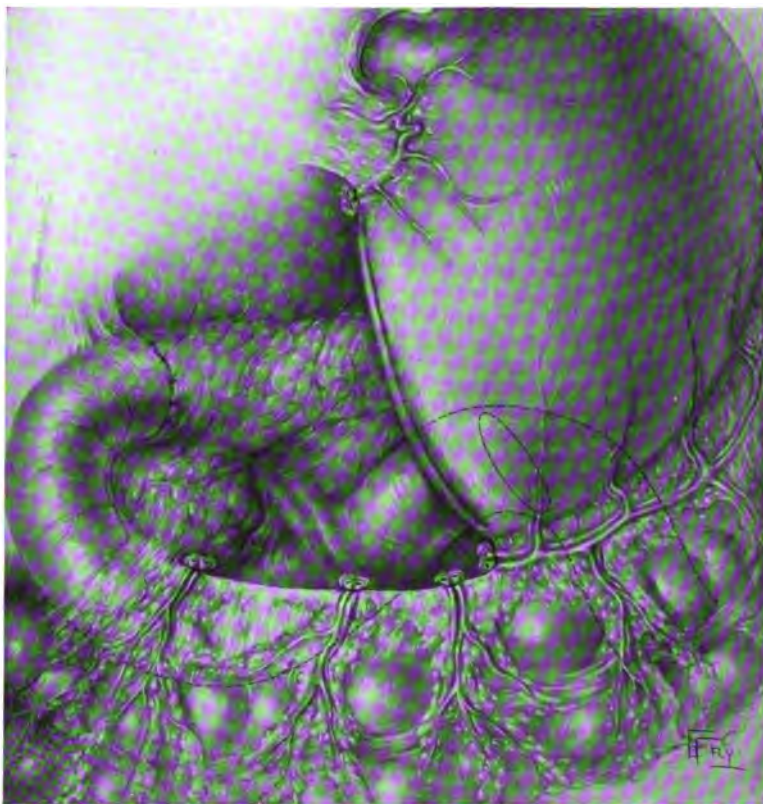


Fig. 114.—Showing operation completed. Closed end of duodenum buried in excavation in pancreas.

terior peritoneum and adventitious sheath of the pancreas are then sutured to the anterior surface of the duodenum. We have used this method for something like six years and have not had leakage in a single instance, either from the duodenum or from the pancreas.

Fig. 113 shows the end of the duodenum closed by purse-string

sutures and the vessels tied in the excavation in the pancreas. Fig. 114 shows the end of the duodenum fastened in the wound in the pancreas.

Ulcers of the posterior wall of the stomach often perforate and become attached to the pancreas. In a previous paper I described a method of transgastric excision of such ulcers. These ulcers usually form an excavation into the body of the pancreas, and it is necessary to excise them cleanly well down into the pancreatic tissue, leaving no area of infection. This opening cannot be closed by sutures, and after stopping the hemorrhage with catgut on a needle, a piece of the gastrohepatic or gastrocolic omentum is mobilized and turned into the excavation in the body of the pancreas, being held in place by catgut sutures. In our earlier cases we used a drain of folded rubber tissue, but abandoned it as unnecessary, since no drainage followed.

## II. INJURIES TO THE PANCREAS IN THE COURSE OF OPERATIONS ON THE SPLEEN

In 31 splenectomies performed in our clinic the tail of the pancreas was injured three times, owing to the fact that the tail passes with the splenic vessels well up into the hilum of the spleen. In performing splenectomy the spleen is withdrawn from the abdomen, the adhesions to the diaphragm and region of the left kidney are separated, and a rubber-covered clamp of the Lower variety is used to catch the entire pedicle. The tail of the pancreas is often so closely incorporated with the pedicle of the spleen that it occasionally is injured. This occurred in three of our cases.

In one case about  $1\frac{1}{2}$  inches of the tail of the pancreas was found attached to the removed spleen and the pancreatic duct was plainly visible in the ligated stump. After covering the stump with peritoneal tissue and attaching a drain (which was unnecessary, since no drainage followed), it was allowed to drop back into position. The patient recovered.

In the second case the tail of the pancreas was found tied in the pedicle about an inch from the tip. Since the case was one of splenic anemia and the patient in poor condition, the stump was allowed to drop back in this condition. The patient recov-

ered. The third case (A77736) was a male, aged twenty-six years, in whom a diagnosis of splenic anemia had been made. At operation (January 14, 1913) the spleen was found to be of great size, extending well to the right of the median line and down to the brim of the pelvis. On account of the adhesions it was unusually difficult to remove the spleen from the abdominal cavity. The clamp was applied and the organ cut away. Catgut ligatures were applied to the splenic pedicle in sections. As the ligatures were tightened on the splenic artery, which was large, tortuous, and atheromatous, it cut through and, with a gush of blood, dropped down behind the pancreas. It was caught with the fingers and compressed against the body of the pancreas, while a second ligature was applied. This cut through also and it was evident that the splenic vessels would not maintain a direct ligature. A double catgut strand was therefore placed around the entire body of the pancreas, about three inches from the tail, including the splenic vessels, the pancreas being used to strengthen the walls of the vessels. The pancreatic tissues were considerably crushed as the ligature was pulled taut. The hemorrhage was controlled immediately, but as softening of the pancreatic tissue with loosening of the ligature was feared, a second ligature was applied in the same manner but one inch farther to the right. It is probable that complete separation of four inches of the pancreas from the head and remainder of the body occurred. The patient made a good recovery and left the hospital in two weeks.

Coffey demonstrated experimentally that tying the pancreatic duct with or without the surrounding pancreatic tissue would not permanently occlude the pancreatic duct, that the duct would regenerate and reunite within a few days. While the duct itself was not actually tied, the pressure of the ligatures about the pancreas must have been sufficient to obstruct its lumen mechanically. The abundant supply of blood from numerous sources prevented serious damage to the nutrition of the portion of pancreas cut off by the pressure of the ligature.

### III. RESECTION OF HALF THE PANCREAS FOR TUMOR

CASE NO. A68699.—J. L., female, aged thirty-seven years. Date of operation, June 15, 1912. History of severe attacks of pain extending into the left abdomen and left lumbar region,



so severe at times as to necessitate the use of morphin. At no time was the patient free from pain. Point of tenderness over the region of the body of the pancreas. Loss of weight, 17 pounds. Duration of illness, three months. Contents of stomach, stools, blood, and x-ray negative. Tentative diagnosis, cholelithiasis with pancreatic involvement. An exploratory incision was made two inches to the right of the median line in the upper rectus muscle. There were no gall-stones, but a hard, irregular tumor the size of an egg was found in the body of the pancreas about its middle. A second working incision was made through the upper rectus muscle, three inches to the left of the median line. The gastrocolic omentum was divided, the stomach drawn upward, and the transverse colon downward. The body of the pancreas and the tumor were brought to the surface as well as possible. It seemed best to begin at the tail and remove the left half of the pancreas with the tumor. This proved to be a difficult procedure since the entire pancreas was deeply placed and fixed in position. One of the deep veins was injured and a free hemorrhage occurred which was difficult to control without injury to the splenic vessels. Finally the tail and body of the pancreas, with the tumor, about  $4\frac{1}{2}$  inches in all, were separated, a strong clamp applied across the body one inch to the right of the tumor, and the left half of the pancreas with the tumor cut away. Four clamps had previously been attached to vessels in the deep portions of the wound. An attempt was made to tie off one of these clamps with catgut on a needle, and a fresh point of bleeding which required another clamp was the result. The handles of the five clamps and the handles of the clamp previously placed across the body of the pancreas were brought to the surface and the cavity from which the pancreas had been removed was packed loosely with gauze. On the fourth day the clamps were loosened and on the fifth day they were removed. The gauze was removed on the tenth day. The patient made a good recovery, regained her normal weight, and remains well. The tumor, which had the external characteristics of a malignant growth, proved on section to be a benign, thick-walled, trabeculated cyst buried in sclerosed pancreatic tissue.

Resections of the pancreas for tumor have seldom been made, although as far back as 1884 Billroth removed the pancreas for an adenocarcinoma, with recovery of the patient. Finney collected 16 cases from the literature in which the pancreas had been

removed for tumor, and he reported a most interesting one of his own. There were 9 recoveries and 8 deaths in the series. All the fatalities occurred in cases of resection for malignant disease. In Finney's case and in two others a complete resection, including the tumor, was made and the divided ends of the pancreas resutured, with recovery of the patients.

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## CLINICAL NOTES ON PATIENTS FROM THE MIDDLE NORTHWEST INFECTED WITH ENTAMEBAS \*

H. Z. GIFFIN

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In 1911 Sistrunk published our earlier experience at the Mayo Clinic with regard to the finding of intestinal parasites in individuals residing in the middle Northwest. Since then the examination of the stools in certain cases has led so frequently to the identification of entamebas that we have come to consider this infection as a relatively common one. In the diagnosis of the different types of amebas present Craig's description of the morphologic characteristics has been followed in our laboratories by Sistrunk and Sanford. Moreover, the recent work of Darling and Craig on the identity of *Entamoeba tetragena* with *Entamoeba histolytica* inclines us to prefer to group cases in which a morphologic diagnosis of either one of these parasites was made as *Entamoeba histolytica*. In this review, however, the former distinctions between *tetragena* and *histolytica* are maintained because of any interest that may remain in connection with the morphologic type of those amebas found in the northern States.

During the last two and one-half years the stools of 1700 patients have been examined for parasites. Entamebas have been found in 227 of these, or 13 per cent. Of this number, 148 were diagnosed as *Entamoeba coli* and 79 as *Entamoeba tetragena* or *Entamoeba histolytica*. These totals include patients from all parts of the country who have been under our observation. This consideration, however, will be confined entirely to those with

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residence in Minnesota, Iowa, Wisconsin, North and South Dakota, Montana, and Nebraska, whose infection, as nearly as can be judged, was not obtained in the South. Most of these patients had never been in the South. A few had traveled in the South, but their visit seemed to have no relation to the onset of their symptoms. The first part of this paper is concerned with a consideration of those cases in which *Entamoeba tetragena* and *Entamoeba histolytica* were present; the latter part with a consideration of the cases showing *Entamoeba coli*.

#### CASES IN WHICH *ENTAMOEBÆ TETRAGENA* OR *ENTAMOEBÆ HISTOLYTICA* WAS FOUND

Of the 79 patients showing *Entamoeba tetragena* and *Entamoeba histolytica*, 41, or a little less than one-half, evidently received their infection while residing in the before-mentioned States and therefore constitute the most important group for our immediate consideration. Of this number, there were from Minnesota 14, Iowa 12, North Dakota 5, South Dakota 5, Nebraska 2, Wisconsin 2, and Montana 2.

Of the 41 patients, 36 showed *Entamoeba tetragena* and only 6 *Entamoeba histolytica* (one of these, a patient with very severe symptoms, showed both *tetragena* and *histolytica*). It is, therefore, a prominent fact that the parasite of predominance conforms morphologically to the description of *Entamoeba tetragena*. In those cases showing *Entamoeba histolytica* the parasites were more numerous, though it is quite certain that these patients did not receive their infection in the South.

In a consideration of the clinical symptoms of these cases the original chief complaint of the patient becomes an interesting basis for classification.

*Group 1.—Patients Complaining Chiefly of Diarrhea.*—Twenty-four of the 41 patients complained chiefly of diarrhea. Thirty-five patients of the 41, however, gave a history of diarrhea, although in some of these it was not their chief complaint. Thirteen had had, at one time or another, severe attacks of diarrhea, with

more or less blood in the stools. As nearly as can be judged, however, these attacks were not so violent as those in cases reported from the South. On the other hand, most of our patients gave a history of more or less constant diarrhea of a mild type, also quite in contrast to the southern cases. More than one-half the patients gave a history of the passage of macroscopic blood at one time or another in the course of their disease.

*Group 2.—Patients Presenting Themselves Chiefly on Account of Abdominal Pain.*—A second group of cases consists of those patients who complained chiefly of abdominal pain—9 in number. It has been our custom to send patients complaining of indefinite abdominal symptoms for a stool examination, and the finding of parasites in this group of cases is due to that routine. The findings, of course, may be accidental, although at least two patients of this group are well of their original complaint.

Three-fourths of the patients (32) gave abdominal pain as a minor complaint. Pain was not confined to the lower abdomen; 10 of the number suffered from upper abdominal pain and 6 complained of pain in the right lower quadrant, suggesting the possibility of involvement of the cecum. Rectal pain was a prominent symptom in 4 patients.

*Group 3.—Those Complaining of Indefinite Gastric Symptoms.*—Patients complaining of indefinite gastric symptoms have often been referred for stool examination. Three patients in the series who consulted a physician chiefly on account of gas and sour eructations, nausea, and epigastric distress, have shown pathogenic entamebas. Complaint of this character, however, is not uncommon in the other cases. Fifteen of the 41 patients gave a history of gastric symptoms, although they complained chiefly of abdominal pain or diarrhea. Nausea seems to be quite commonly associated with the more severe attacks, 11 of the series volunteering this information.

*Group 4.—Patients with Constipation.*—It is rather not to be expected that *Entamoeba tetragena* should be found in patients complaining chiefly of constipation and without diarrhea. In two instances of this character, however, amebas were easily demon-

strated. Intermittent constipation, even in connection with those cases showing severe diarrhea, is not an uncommon finding.

*Group 5.—Miscellaneous Cases.*—In the remaining three cases dyspnea and weakness were given as the chief complaints and were the result of severe anemias. Two of these anemias were definitely of the pernicious type, while one was of doubtful nature and may have been entirely secondary. The finding of entamebas in cases of pernicious anemia can be regarded as only accidental.

Only one case of abscess of the liver has been observed among patients from the middle Northwest. In this instance *Entamoebæ histolyticæ* were demonstrated in the stools; the abscess, which was drained, was of typically amebic character. The patient resided in Duluth, had never been in the South, and gave a six weeks' history of diarrhea with bloody stools. It is not certain that this patient received his infection in Minnesota. He had emigrated from Russia six months previously, but his history had been of only six weeks' duration.

The duration of the history relative to the bowel symptoms for the entire group of 41 patients varied from six weeks to twenty years. In 6 of the patients it was longer than ten years, in 10 over five years, while in 17 it was less than a year; the average was four years.

The eosinophil count was low. Three of the series showed no eosinophils on differential count; the average in 21 counts was only 2.5 per cent. In this connection it may be of interest to note that 13 patients have been sent to the laboratory on account of a very high percentage of eosinophilia in order that a search for parasites might be made, and in all these instances the results were negative for entamebas.

Proctoscopic and sigmoidoscopic examinations were obtained in 23 of the 41 patients. In 16 they were negative, in 3 a diffuse colitis was demonstrated, in 2 a granular colitis, and in two ulceration. Those cases showing ulceration and diffuse or granular colitis were all infected with *Entamoeba tetragena*. It should be remembered that a negative proctoscopic examination may not necessarily mean a negative colon, as the disease may be localized

at one of the flexures or in the cecum. It is quite likely, however, that the large number of negative examinations is at least another indication of the mild character of these cases in comparison with the infections in the South. From the patient's point of view, however, they are severe enough to be a great inconvenience and detrimental to the general health.

The parasites were usually demonstrated at the first examination. In 31 instances amebas were found at the first examination, in 9 two examinations were necessary, and in one case 3 examinations. It is also evident, therefore, that the search for parasites should not be abandoned too early. In the case in which three examinations were necessary for a demonstration of the parasites the patient had complained of intermittent attacks of diarrhea with bloody stools for four years.

#### CASES IN WHICH ENTAMOEBA COLI WAS DEMONSTRATED

As formerly stated, *Entamoeba coli* was reported in 148 patients. Of these, 106 were in patients residing in the middle Northwest. Fifty-nine, or over one-half of these patients, consulted a physician chiefly because of diarrhea, while in 69, or two-thirds of them, diarrhea was given as one of the principal complaints. One showed granular colitis, 8 diffuse colitis, and 4 ulcerative colitis on proctoscopic examination. Of those presenting themselves chiefly on account of diarrhea, one-third gave a history of more than five years' duration, 9 more than ten years, and 4 more than twenty years. In many of them the diarrhea was severe in character. Thirty-eight, or over one-third, showed red blood-cells on microscopic stool examination, while 16 gave a history of macroscopic blood. The parasites were usually found at the first examination. In only 7 of the 106 patients was a second stool examination necessary for the demonstration of the amebas.

We have no data on which to base a discussion of the possible pathogenicity of *Entamoeba coli*, either positively or negatively, and present these facts only as statements of our findings.

The presence of *Entamoeba coli* in the more severe cases need indicate no etiologic relationship on the part of these organisms.

And again it is quite likely that a further search for parasites would have demonstrated the presence of *histolytica* also in some instances; several of our more recent cases showed *Entamoeba coli* at the first examination and *Entamoeba histolytica*, as well as *coli*, subsequently.

#### TREATMENT

It has been very difficult to obtain an approximately accurate idea of the results of treatment in this series of cases. It has generally been necessary for the patient to return to his home, where the treatment was carried out under the care of the family physician. Ipecac alone was used in 75 per cent. of the cases in which treatment seemed advisable. Ipecac was administered in conjunction with coal-oil enemas to eight patients. This does not take into account the treatment of those patients residing elsewhere than in the middle Northwest. Enemas of kerosene (Hanes) alone were used under our observation in four instances in which *Entamoeba tetragena* or *Entamoeba histolytica* was present (one of these showed ulcerative colitis), and in all of them the results were excellent. It is our impression that coal-oil enemas should be given a trial in cases of entamebic infection in order that we may learn something more definite with regard to their efficacy. The administration of emetin hydrochlorid is considered by many observers of large experience to be almost specific in its action, and is especially indicated in severe types of infection (Rogers).

It may be emphasized that amebas are generally demonstrated easily at the first examination if the patient be properly prepared and the stool properly obtained. Epsom salts may be given early in the morning, and an hour or two later the patient reports at the laboratory, where one or more stools may be examined while they are yet warm. It is a noticeable fact that the search may be difficult either in a stool that is too well formed or in one which is too watery.

It may be well to urge a more wide-spread interest in the examination of stools for parasites in the northern States. Undoubtedly entamebic infection is a quite generally unrecognized



cause of diarrhea, and probably of certain indefinite abdominal complaints. At the same time it should be remembered that the finding of parasites can be regarded only as a part of the evidence in the diagnosis of any condition of the bowel; there may be a tendency to ascribe a patient's complaints too quickly to this finding.

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## CLINICAL VALUE OF STOOL EXAMINATIONS \*

A. H. SANFORD

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It is quite generally acknowledged by clinicians that there should be more stool examinations in routine clinical work, and yet there seems to be a continued tendency to avoid this branch of laboratory technic.

It is not my purpose, in this paper, to go into details of the technic, since this subject is sufficiently covered in the various textbooks. However, it is to be hoped that by emphasizing certain points the practical nature of the examination of feces may be seen, and that the possible diagnostic value of the procedure in any practitioner's hands be not underestimated.

In less than three years about 2000 stool examinations have been made in the Division of Bacteriology and Parasitology of the Mayo Clinic. A large proportion of patients in this series of cases were suffering from diarrhea due to various causes. In 511 of the cases parasites of some type were found. There were 135 tests for pancreatic function, and many tests were made merely for occult blood; a large number of all tests were negative.

*Preparation of Patients.*—The preparation of the patients for stool examination varies with the nature of the examination indicated. Schmidt has suggested a diet to be fed patients before routine examinations. However, it does not seem entirely feasible rigidly to follow this. Schmidt's patients are instructed to eat five times a day instead of three, and the quantities of food are arranged accordingly.

If the stool is to be examined for digestive function, a general mixed diet is ordered the day before, that is, a patient who has

\* Read before the Wisconsin Med. Soc., October 2, 1913. Reprinted from the Wisconsin State Medical Journal, April, 1914.

been on a restricted diet is ordered to eat a small amount of meat, potatoes, bread, butter, milk, etc. As a laxative, he is given one grain of calomel and five grains of phenolphthalein the night before the examination.

Before examining the stool for occult blood the patient is kept on a meat-free and chlorophyl-free diet for twenty-four hours. No laxative is given, but a normal stool is examined by the usual chemical methods.

The routine preparation before examining for parasites is important. There is no prescribed diet. On the morning of the stool examination the patient takes one or more tablespoonfuls of Epsom salts before breakfast; then, after eating, comes to the laboratory for his stool. This is collected, free from urine if possible, in a vessel, and examined at once.

#### EXAMINATIONS

**DIGESTIVE FUNCTION.**—In examining the stool for evidence as regards digestive function, the appearance is first noted: color, consistence, bulk, etc. A “pancreatic” stool is often described as a light yellow, bulky, frothy stool, with an excessive amount of undigested fat, as evidenced by the greasy appearance. For the detection of the presence of bile-pigment the Schmidt test is reliable and easily performed. Bile derivatives are shown by adding saturated  $\text{HgCl}_2$  to a small portion of the stool. Hydrobilirubin or urobilin is shown by the mixture turning pink. A green color indicates the presence of bilirubin. Neutral fats are shown by staining with Sudan III. Fatty acid crystals, starch granules, meat-fibers, red blood-cells, and pus-cells are readily recognized microscopically.

For the functional activity of the pancreas there is no test absolutely specific. Up to the present time 135 Wohlgemuth tests have been made in the Mayo Clinic, with somewhat varying results.

Briefly, this test is performed by weighing out 5 grams of stool, extracting thirty minutes with salt solution, and centrifuging sharply fifteen minutes, or until sedimentation is complete. We

have noted the ratio between supernatant fluid and sediment, and using this as a factor in the final estimate of units of diastase per grams solid matter. To be sure this makes the method roughly quantitative. After filtering the fluid portion it is placed in test-tubes as follows: 2 c.c., 1 c.c.,  $\frac{1}{2}$  c.c. of filtrate, then in the next three tubes 2 c.c., 1 c.c.,  $\frac{1}{2}$  c.c. of a 1:10 dilution of filtrate, and in the last three tubes 2 c.c., 1 c.c.,  $\frac{1}{2}$  c.c. of a 1:100 dilution of filtrate. Five c.c. of a 1 per cent. soluble starch solution is added to each tube.\* A small amount of toluol in each tube prevents bacterial action, and incubation is carried on for twenty-four hours. The tubes are filled to the same level with tap-water, and a few drops of Lugol's solution are added. The tube in which erythrodextrin is present is taken as marking the end reaction. One unit of diastase is arbitrarily considered as the amount which digests 1 c.c. of 1 per cent. soluble starch. Then the number of units per cubic centimeter of stool is calculated from the dilution in the tube containing erythrodextrin and the ratio of the fluid to solid matter in the stool extract. Wohlgemuth considers anything below 250 units as subnormal. The number of units in a normal stool may be several thousand.

The test made in our clinic will not be considered in detail in this discussion. I shall merely state that of those cases with less than 250 units of diastase, 23 per cent. showed involvement of the pancreas at operation; 15 per cent. not operated on were diagnosed as having pancreatic disease. However, there were 16 cases, or 26 per cent., of those with less than 250 units of diastase operated on, and no pathologic conditions found in the pancreas. These 16 cases may be grouped as follows: Five cases of cancer of abdominal organs other than the pancreas; 6 cases of gall-stones or common duct involvement; 1 aneurysm of the abdominal aorta; 1 pyloric obstruction; 1 lipoma of the mesentery of the jejunum; 1 chronic appendicitis, and 1 hypertrophic cirrhosis of the liver.

It is apparent, then, that the test is not of absolute diagnostic value, but shows merely the amount of pancreatic enzyme in the

\* Use Kahlbaum or Merck soluble starch only for making this solution.

particular stool examined. A subnormal amount may be due to disease of the pancreas or conditions elsewhere indirectly influencing the amount of secretion reaching the alimentary canal.

*Occult Blood.*—The various tests for occult blood are all well known. Spectroscopic analysis, or the simple chemical tests, can be carried out easily in any laboratory. We are studying the various tests in relation to the diagnosis of cancer and ulcer of the stomach and duodenum. At present there is nothing to add to former statistics. It is generally known that the benzidin test is extremely delicate for slight traces of blood, and that this may really be more of a diagnostic disadvantage than otherwise. The tincture of guaiac test, made with an ethereal extract, while not positive when the altered blood is very highly diluted, is accurate, and the technic so simple that there is no excuse for not making these observations.

*Intestinal Parasites.*—The most important findings in stool examinations are those in connection with a search for intestinal parasites. The presence of ordinary worms is usually reported by the patients themselves, but a careful examination of the stool will at times show the presence of ova when the patient does not realize that he has a parasitic infection. Of the microscopic parasites, the protozoa are the most important from a pathologic point of view. The preparation of the patient has been described. It cannot be emphasized too strongly that the stool must be after a dose of Epsom salts, and that the examination be made at once, a warm stage being used on the microscope.

The flagellates are easily recognized by their rapid, darting motion. *Trichomonas intestinalis* is a pear-shaped flagellate, about 10 to 15 microns in length, and moves forward in a peculiar rotary manner. A similar flagellate, *Cercomonas hominis*, is slightly smaller, more oval in shape, darts about the field, but does not have the rotary motion. We have noted these protozoa 259 times in all, 195 times as the only organisms found, and 64 times in connection with other parasites.

Most text-books are inclined to attach little significance to flagellates as a cause of intestinal disturbance. However, it

should be stated that their presence in great numbers is often associated with diarrhea. Another parasite of this group, the *Lambia intestinalis*, has been observed by us 16 times altogether—14 times in patients that had never been South. Stitt says: "This parasite is considered of little importance, but as it is responsible for a chronic and intractable diarrhea associated with mental and physical depression, it undoubtedly causes an affection only minor in importance to amebic infection."

It is usually believed that dysentery caused by ameba is a tropical disease, or at least confined to our southern states. However, there are so many reports of amebic dysentery in northern latitudes that we cannot look on this disease other than as a universal infection.

There are two types of amebæ found in the stool: One, *Entamoeba coli*, considered non-pathogenic, is usually round, sluggishly motile, ectoplasm clear, central nucleus easily seen. The pathogenic ameba, *Entamoeba histolytica*, is usually a little larger, is actively motile, pushing out long, finger-like or lobose pseudopodia; has a distinct hyaline ectoplasm. *Entamoeba tetragena* has now been definitely identified with *Entamoeba histolytica* (Craig). The nucleus is usually readily seen and is eccentric. In degenerating forms this type is not so readily seen, and this fact gave rise to the idea that there were two types of pathogenic amebæ. Red blood-cells are ingested and may be seen within the organism. They are digested, and the greenish color of some of the amebæ has been thought to be due to the hemoglobin from disintegrated red blood-cells. There is no doubt that we have both types of amebæ in the North.

Up to September 1, 1913, amebæ classified as *Entamoeba coli* had been observed in 176 cases in the Mayo Clinic. Only 17 of these were from the southern States; 159 were from northern States. *Entamoeba histolytica*, including those called *tetragena*, were found in 110 cases; 96 of this number were patients from the north and northwest. Of the pathogenic type, we have had 23 cases from Minnesota, 22 from Iowa, a number from the Dakotas and the Northwest, 4 cases from Illinois, and 6 from Wisconsin.

## CASE REPORTS

CASE 1.—No. A77273; male; aged thirty-four; lives in LaCrosse, Wisconsin. Date of examination, December 12, 1912. Was born in Norway; has lived in Norway, Wisconsin, and the Philippines. Usually drank deep well water. Patient contracted dysentery in the Philippines eleven years ago. Amebæ were found at that time. He is losing weight; passes much blood and mucus. Has 6 to 18 bowel movements daily. Severe pain and tenderness all through the abdomen. Stool loose, brown, and showed fresh blood. Microscopically, trichomonades and many *Entamoebæ histolyticæ* were found.

CASE 2.—No. A54572; female; aged thirty-three; lives in Wisconsin. Patient has never been south. Date of examination, June 15, 1911. Had diarrhea four years previous to examination; four bowel movements daily. Since that time has had two or three movements daily. No blood or mucus seen. Has acute right-sided pain. Examination of stools, June 16, 1911, showed cercomonads and *Entamoebæ histolyticæ* in great numbers. Ipecac treatment was advised, but a report from the patient, received May 10, 1913, stated that the treatment was not carried out, and the present symptoms indicate that she is suffering from amebic dysentery.

CASE 3.—No. A87465; male; aged sixty-five. Farmer, lives in Wisconsin; was born in England, and has never been south. First examined July 10, 1913. Drinks water from a drilled well. For the past thirty years has had attacks of diarrhea three or four times a year, with 8 to 12 bowel movements daily; blood and mucus in the stools. Has vague pain and tenderness all through the abdomen. No loss in weight. Examination showed loose, brown stool, red blood-cells, cercomonads, and *Entamoebæ histolyticæ* (tetragena type). Treatment with salol-coated ipecac pills was instituted, and kerosene enemas administered. Examination July 21, 1913, showed amebæ still present. Another on July 29, 1913, was free from red blood-cells and parasites.

CASE 4.—No. A60544; female; aged twenty-one. Farmer's daughter; has always lived in a small town in Minnesota, a few miles from Rochester. When first examined on October 26, 1911, she had suffered for about one year with a continuous diarrhea; four or five bowel movements daily. She had been operated on for appendicitis ten months previously. Had lost 26 pounds in weight,

and was extremely nervous. No blood seen in the stools, but mucus occasionally. Many actively motile amebæ, tetragena type, were reported October 26, 1911. Ipecac treatment has been carried out, with only partial success. A report on November 12, 1911, shows no parasites. This was immediately following ipecac treatment, however. In reply to a letter of inquiry the patient stated, on May 10, 1913, that she still has two or three stools a day, with mucus, and at times suffers with abdominal pain. Her general health is much improved.

These are typical histories taken at random, and show the type of cases in which these parasites are found. It should also be mentioned that we have had one patient who has never lived out of Minnesota in whom *Balantidium coli* was found. This is one of the infusoria, a typical genus of the order Heterotrichida, and has been frequently reported in the tropics as a cause of severe ulceration of the bowel, at times causing death.

In conclusion, I would make a plea for more consideration of the clinical value of a systematic stool examination. A simple technic is all that is necessary or desirable, and the finding of a parasite that may possibly be the cause of an obstinate bowel disturbance will surely repay one for the time spent. We have been schooled to believe that amebic dysentery is a tropical or subtropical disease. To be sure, we see it in its more severe forms in those climates where the resistance of the patient is lowered to all types of infection. Text-books are published annually with antiquated ideas borrowed from previous publications, and erroneous ideas are thus perpetrated. We should realize that intestinal parasites in the north are of great importance, and that there are still many problems to be solved in the field of parasitology.

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## FACTORS OF SAFETY IN INTESTINAL SURGERY \*

CHARLES H. MAYO

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In all intestinal surgery there exist certain factors of safety which, if carefully taken into account, may serve to increase both not only the patient's comfort, but also his chance of ultimate recovery. Many of these are at first thought so simple that they are sometimes overlooked by both the attending physician and the surgeon, and it is the purpose of this paper to call attention to some of the more important ones.

*Gastric Dilatation.*—Without clinical experience one might conclude, from the articles written on gastric dilatation following operations in the abdomen, that the condition was a rare one and associated with a high mortality. It is possible that only the severe types of the condition have been recognized. If the stomach-tube be passed in the abdominal case which is not progressing favorably, even though fluids are being taken without vomiting, one will be surprised to find how often there is a considerable degree of dilatation. It is, in fact, a very common complication, though, fortunately, usually only temporary. In the treatment of these cases the stomach should be kept empty by washing it out at least every four hours for three or four times, or until the contents show that a longer interval will suffice. In order that the congestion of the superior mesenteric artery may be relieved, the patient should be turned on his side, or even upon his abdomen. This procedure is second in importance only to keeping the stomach washed and empty.

\* Read before the St. Louis Med. Soc., December 20, 1913. Reprinted from *Old Dom. Jour. of Med. and Surg.*, 1914, vol. xviii.

*Gastro-enterostomy.*—In the performance of anterior gastro-enterostomy the usual rule has been to allow the loop of jejunum to hang directly from the circle of the opening into the stomach. Hartman's method is of great advantage in preventing the angulation or spur occurring at the fold of bowel, which often throws an undue amount of bile into the stomach. This consists of placing an additional suture or two, uniting the intestine to the stomach one inch on either side of the opening. The bowel thus runs past the opening in the stomach instead of hanging from it. In this connection may be mentioned the necessity of suturing the opening in the mesentery of the transverse colon to the gastric side of the posterior gastro-enterostomy to prevent obstruction by hernia through this structure.

In resecting the pyloric end of the stomach the surgeon occasionally finds that the duodenum is free and the stomach quite movable, and he is deterred from employing the so-called Billroth No. 1 operation of union of the duodenum and of the gastric section, which is only one-third or one-half filled by the end of the bowel. The triangle of union of stomach and intestine is the so-called "fatal suture angle," and because of the high mortality following this procedure the operation has been practically abandoned. However, it occasionally becomes a useful procedure, and the danger is overcome by making a  $\frac{1}{2}$ -inch incision of the bowel opposite the mesentery, placing the end of the bowel at the lower end of the stomach and suturing the duodenum on either side of the line of the gastro-intestinal section, the external row of the gastroduodenostomy suture-line being continued around the opening of the stomach, completely covering and protecting the whole of the gastric suture line. The same method is occasionally of advantage as a posterior gastro-enterostomy, using the side of the jejunum drawn through the mesentery of the transverse colon, the suture line being united to the edges of the mesenteric opening at the close of the operation.

*Jejunostomy* is an operation which has a distinct place in the surgery of the upper abdomen, and in certain cases replaces gastrotomy; the latter, of course, being the best method of feeding in

complete and in malignant esophageal obstruction, and also when the obstruction is due to growth in the cardiac end of the stomach, preventing the passage of food from the esophagus. Where a great amount of the stomach is involved, its digestive fluids need not be considered of importance, and any food put into it occasions painful peristalsis. In such cases the Witzel or Stamm Kader method of inserting a rubber tube into the jejunum, which is attached to the abdominal wall at the point of entrance, makes a very effective method of feeding. We have also employed this in some cases of acute perforating ulcer of the stomach or duodenum. Its use here, however, is temporary, and if the operation is properly done, there will be no leakage upon the withdrawal of the tube. The adhesions of the jejunum to the abdominal wall some 14 inches down from its origin seem to cause no trouble.

*Enterostomy.*—It may be well to emphasize the good effects of enterostomy as a safety-valve in obstruction of the bowel following abdominal operations. The procedure is a simple one of itself, and life-saving in a large percentage of cases where the conditions are recognized, and the procedure applied before it is too late. As a rule, it should be instituted by the end of the third or possibly as late as the fourth day. The fifth day and later will often prove too late. Usually no general anesthetic is required—a local application of 0.5 per cent. novocain and a little adrenalin will be sufficient. As a rule, upon reopening the wound the distended bowel comes into the opening and a tube can be inserted. Sometimes it is advisable to puncture with a needle to permit the escape of gases before inserting the tube. Occasionally the obstruction is in the large bowel, and an appendicostomy will serve the purpose of bowel drainage. Some of these cases are due to paresis, which is of a temporary nature. Some of them are due to kinks and adhesions, with inefficient peristalsis to overcome them. If the patients survive twenty-four hours following the insertion of the tube, most of them will recover. The difficulty, whatever it may be, passes off, and but few of them require further operative procedure than the enterostomy. However, should it be necessary, their improved condition will permit it within a short time.

If the opening is jejunal, rectal fluids will be necessary in addition. If it be low in the ileum, sufficient nourishment is readily assimilated.

McArthur has proved the advantage of using the cystic and common ducts of the liver for patients requiring fluid, which cannot be administered by the stomach or rectum. The possibility of using the appendix as a feeding tube is also worthy of consideration, while its use as a safety-valve to permit the escape of fluids and gases caused by obstruction of the transverse, ascending, or descending colon is of the utmost importance in tiding patients over temporary periods of obstruction.

*Obstruction of the Colon.*—In many cases of cancer of the large bowel a sudden obstruction may occur without appreciable warning to the patient. Such patients are often brought to the operating-room in an almost moribund condition. No opportunity is afforded to carry out Roentgen tests as to location, etc., the emergency of the case demanding immediate relief. If a fair idea of the location of the obstruction be obtained, an incision over this region is advisable for examination. A small right incision is then made, the appendix drawn out, and its mesenteriolum caught by suture. Thick vaselin is applied around it and in the incision to protect against absorption. The base of the appendix should fill the incision. The tip may now be amputated, and a catheter passed through into the cecum. This at once relieves the gases anterior to the obstruction (Fig. 115). The outer leaf of parietal peritoneum connected with the colon has no blood-vessels, nerves, or structures of any importance, and can be freely incised to mobilize the colon. In many cases it is best to use the Mikulicz two-stage method, drawing out the fold of colon, including the tumor, and amputating at the end of several days. The reestablishment of the lumen does not require secondary opening of the abdomen, but is done by pressure with forceps. When there is an accumulation of gas below the stricture, or when it is advisable to insure the safety of a suture line in resecting the colon, it is sometimes of advantage not only to use the appendicostomy for the release of gases in the an-

terior bowel, but, in addition, a thorough divulsion by stretching the sphincter ani and rectum in order to obtain absolute relief of

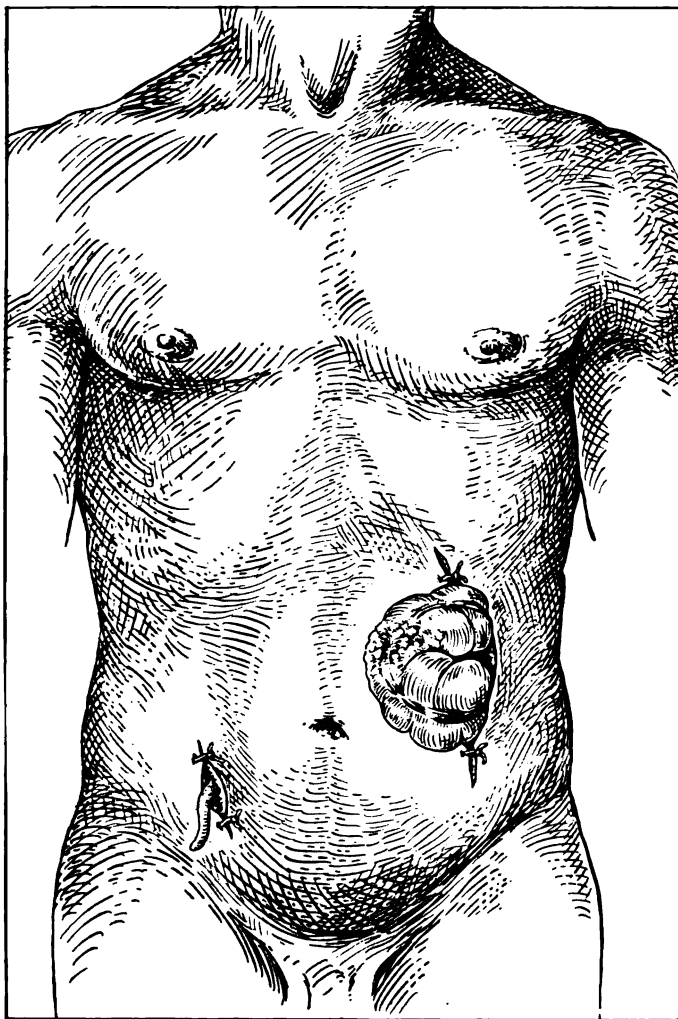


Fig. 115.—First stage of the Mikulicz colostomy for colonic carcinoma with appendicostomy for drainage.

tension on the suture line. When the Mikulicz two-stage method can be employed for the resection of cancer of the large bowel, it

certainly is one of the safest procedures, although the convalescence may be considerably longer than by other methods.

We find advocated in the literature the use of fatty tissue in surgery, both for filling defects and in preventing the serious results of adhesions. In the surgery of the gall-bladder and ducts, probably one-third of the patients are prevented from the complete enjoyment of health and comfort because of adhesions of the stomach, pylorus, or duodenum to the liver or parietal wall or the gall-bladder. These adhesions are the cause of serious symptoms in many cases. After completing the operative procedure, before closing the abdominal incision, the relation of the pylorus and duodenum to the traumatized abdominal area should be observed. It will be found advisable in many of the cases to build a fatty apron to protect this area, using the fatty round ligament and the gastrocolic and hepatic omentums. Should adhesions take place to such fatty tissue, no harm will result. In operating for secondary adhesions we recommend covering the separated surfaces of fixed organs with fatty tissue, and the free application of vaselin to prevent early adhesions from lymph organization before peristalsis is resumed. In secondary operations much painstaking but useless effort is often made to separate adhesions of fatty tissues. Often such surgery is harmful, as the new adhesions may not form as favorably as those separated.

In the posterior extirpation of the rectum for cancer the end of the sigmoid should be left tied to obstruct for three days. Whether it be left as a sacral anus or be drawn through the anal ring and attached around this structure, primary contamination of the surface of the wound is prevented and healing greatly hastened.

#### REFERENCE

McArthur: New York Med. Jour., January 27, 1912, pp. 168, 169.

## THE FREQUENCY OF CARCINOMA OF THE APPENDIX\*

WM. CARPENTER MACCARTY AND BERNARD FRANCIS  
McGRATH

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The frequency with which carcinoma of the appendix occurred in the surgical material of the Mayo Clinic during a routine examination of appendices which had been removed primarily or secondarily, has stimulated the writers to investigate further the regularity and frequency of its occurrence. In a previous report† 22 specimens which presented histologic pictures of carcinoma occurred in 5000 specimens. Only 5 of these were large enough to be suspected at operation. The remaining 18 were discovered only upon making routine gross serial sections. The neoplasm was not visible upon the external surface, and occurred always in appendices in which the lumen had been partially or completely obliterated.

In the published series the condition occurred in the following frequency:

- 5 (0.5 per cent.) in the first 1000.
- 7 (0.7 per cent.) in the second 1000.
- 3 (0.3 per cent.) in the third 1000.
- 2 (0.2 per cent.) in the fourth 1000.
- 5 (0.5 per cent.) in the fifth 1000.

The youngest (five years) occurred in a female who was operated upon for appendicitis. The average age was thirty years. Seventy-three per cent. were females. Ninety per cent. occurred near the tip of the appendix.

\* Reprinted from *Annals of Surgery*, lix, 1914.

† MacCarty and McGrath: "Clinical and Pathological Significance of Obliteration, Carcinoma and Diverticulum of the Appendix," *Surgery, Gynecology, and Obstetrics*, March, 1911.

It was found that the average duration of symptoms was 3.3 years. One in every 225 of all appendices in the series and one in every 53 partially or completely obliterated appendices were carcinomatous. Thirty-one per cent. was found in association with other abdominal and pelvic conditions.

Since these findings were made, a series of 3039 specimens which



Fig. 116.—(No. 31005.) Involvement of the submucosa and the musculature by carcinoma.

were removed between November 15, 1911, and July 1, 1913, have been examined immediately upon removal. In this later series there were 18 (0.6 per cent.) carcinomatous specimens, in all of which the lesion occurred at or near the tip in a portion, the lumen of which had been obliterated. In none of these was there any gross evidence of the condition at operation. The findings were made only upon careful examination in the surgical laboratory.



The lesion itself consists of islands or masses of epithelial cells, which are scattered throughout the submucosa, muscularis, and subserosa (Figs. 116 and 117).

The nuclei present the irregularities which are characteristic of carcinomatous cells (Fig. 117).

The present interest which stimulates this report rests upon a desire on the part of the investigators to learn something about the clinical significance of the condition.

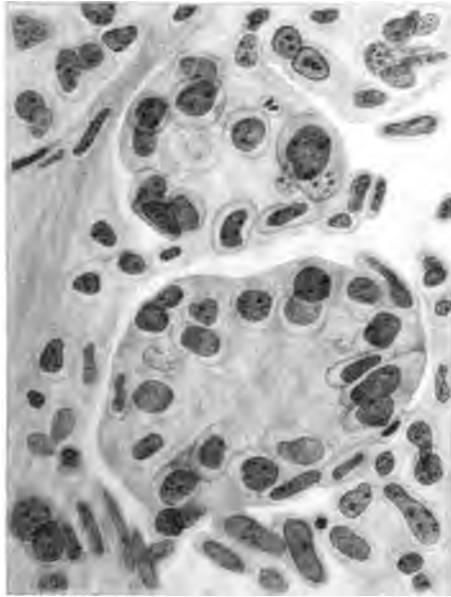


Fig. 117.—(No. 31005.) Showing the irregular character of the nuclei in early carcinoma of the appendix.

In none of the cases herewith presented was there any fact which pointed to clinical importance. However, the mere fact that such a condition is comparatively frequent, and, indeed, rather a constant finding, is significant enough to warrant closer study of the appendix in view of the possibility of more extensive changes.

Surgeons and pathologists are therefore urged to examine closely all such cases and note the presence of metastases if such occur.

TABLE OF CASES

HOSP. No.	AGE	SEX	DURATION OF SYMPTOMS	LOCATION OF PAIN	FEVER	VOMITING	JAUNDICE	CONDITION FOUND
28043	26	F.	4 years.	Right iliac region.	+	..	..	Chronic appendicitis.
28359	50	F.	15 years.	Umbilical region. Right iliac region.	..	..	..	Chronic appendicitis. Tumor on the end of appendix. Carcinoma.
26527	25	F.	4 years.	Epigastrium.	..	..	..	Chronic cystic appendicitis.
18030	33	M.	2 years.	Right iliac region. Abdomen (general). Right iliac region.	+	+	..	Cirrhosis of liver. Carcinoma at base of appendix.
17259	20	F.	Several years.	Right iliac region.	..	..	..	Subacute appendicitis. Carcinoma of tip of appendix.
31005	23	F.	8 years.	Right iliac region, to back.	..	..	..	Chronic appendicitis.
25862	50	M.	1 year.	Abdomen (general). Right iliac region.	+	+	..	Chronic appendicitis.
31023	37	F.	4 years.	Umbilical region.	+	+	..	Chronic appendicitis. Gall-bladder thickened.
31326	26	F.	8 years.	Right iliac region. Right hypochondrium.	+	+	..	Chronic appendicitis.
31679	5	F.	Since birth.	Right iliac region.	..	+	..	Chronic appendicitis. Enlarged glands in the mesentery.
32898	22	F.	8 months.	Right iliac region.	+	+	..	Chronic appendicitis.
29615	27	F.	7 weeks.	Right iliac region. Right hypochondrium.	..	..	+	Chronic appendicitis (adherent).
24497	42	M.	3 months.	Epigastrium.	..	..	..	Right inguinal hernia. Chronic appendicitis.
34532	80	M.	10 years.	..	..	..	..	Four stones in urinary bladder.
A39079	..	F.	..	..	..	..	..	Subacute appendicitis. Cholelithiasis.
32682	34	F.	4 months.	Right iliac region.	..	+	..	Endometritis and uterine fibroids. Appendicitis, carcinoma of the tip.
31580	16	F.	2 years.	Right iliac region.	+	..	..	Acute appendicitis.
21362	29	M.	10 days.	Right iliac region.	+	+	..	Acute appendicitis. Small abscess in omentum.
23045	26	F.	1 month.	Right iliac region.	..	+	+	..
23045	26	F.	2 years.	Right hypochondrium.	..	+	+	..
Carcinoma A.	..	..	..	..	..	..	..	..
Carcinoma B.	..	..	..	..	..	..	..	..
Carcinoma C.	..	..	..	..	..	..	..	..
45694	22	F.	6 months.	Epigastrium.	..	..	..	Carcinoma of the appendix.
43935	44	M.	15 years.	Epigastrium.	..	..	..	Chronic catarrhal cholecystitis.
								Chronic pericholecystitis.
								Chronic catarrhal appendicitis with stenosis of canal in distal third and carcinoma of tip.
44138	10	M.	9 months.	Lower left quadrant.	..	..	+	Chronic catarrhal appendicitis with carcinoma developing on area of stenosis at middle and causing atresia of canal.
44170	37	F.	5 years.	Lower abdomen.	+	..	..	Bilateral chronic suppurative salpingo-oophoritis. Very early carcinoma of appendix.
44255	36	F.	5 years.	Epigastrium.	..	..	..	Colloid carcinoma of appendix.
44537	27	F.	11 years.	Right iliac region. Epigastrium.	..	..	+	Adenomyoma of uterus.
45406	31	F.	11 years.	Epigastrium.	..	+	..	Chronic catarrhal appendicitis with carcinoma at tip.
								Carcinoma of appendix. Chronic catarrhal cholecystitis. Cholelithiasis.

TABLE OF CASES—(Continued)

HOSP. No.	AGE	SEX	DURATION OF SYMPTOMS	LOCATION OF PAIN	FEVER	VOMITING	JAUNDICE	CONDITION FOUND
45446	39	F.	8 years.	Right iliac region.	..	..	..	Carcinoma of appendix. Umbilical hernia.
47148	22	M.	2 years.	Right iliac fossa.	..	..	..	Chronic catarrhal appendicitis with carcinoma at tip.
48430	17	F.	8½ months.	Right iliac fossa.	..	+	..	Carcinoma. Chronic catarrhal appendicitis with obliteration of distal third.
48974	27	M.	4 years.	Epigastrium.	..	..	..	Carcinoma 5 mm. from tip of appendix.
48974	30	M.	7 years.	Epigastrium.	..	..	..	Chronic catarrhal appendicitis with carcinoma at tip.
49976	28	F.	3 years.	Right iliac fossa.	..	+	+	Small hemorrhagic fibromyoma. Chronic catarrhal appendicitis with carcinoma at tip.
50920	10	F.	4 years.	Right iliac fossa.	+	..	..	Chronic catarrhal appendicitis with carcinoma at tip.
51904	34	M.	4 days.	Under right costal arch.	..	+	..	Carcinoma.
52076	32	F.	2 months.	Right iliac fossa.	..	..	..	Bilateral chronic salpingitis and oöphoritis. Appendix-carcinoma.
53526	26	F.	18 years.	Abdomen.	..	+	..	Carcinoma of distal end and pigmentation of mucosa of proximal one-half.
54098	44	F.	7 months.	Right of umbilicus.	..	..	..	Bilateral chronic salpingitis. Simple ovarian cyst. Chronic catarrhal appendicitis with obliteration of mucosa at tip. Carcinoma at tip.

## RESECTION OF THE RECTUM FOR CANCER WITH PRESERVATION OF THE SPHINCTER \*

CHARLES H. MAYO

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The large bowel is quite commonly affected with cancer, especially the cecum, ascending colon, sigmoid, and rectum. While it is unfortunate that in the majority of cases of cancer of the large bowel the patients are late in receiving surgical treatment, it is fortunate that such a malignant process may remain for a long time a local one. The lymphatics in this structure, except in the lower rectum, are few as compared with those of the small intestine and other abdominal organs. The inflammatory and cicatricial zone which surrounds such areas of ulceration acts as an effective coffer-dam. In fact, such inflammatory deposits often lead to early diagnosis of the true condition, and many cancers of the sigmoid and rectum considered hopeless at the time of a colostomy have, within a short period, become so much reduced that a radical extirpation has been possible later. Extirpation of the cecum and ascending colon for cancer has given a high percentage of cures because an anastomosis of the ileum into the colon is an ideal enterostomy for delivering semi-liquids. Malignant growths of portions of the large bowel other than the rectum are often extirpated and treated by immediate suture. As to the choice of a method of operation, each case must be considered individually. The Mikulicz method, a two-stage resection in the movable colon, is probably more commonly employed now than formerly, except in cancer of the cecum. This is one of the safest known methods, although the convalescence following is somewhat more protracted.

\* Read before the Southern Surg. and Gynec. Assoc., Atlanta, December 16-18, 1913. Reprinted, Surg., Gyn., and Obst., 1914, xviii.

Cancers of the rectum in which not more than 8 inches of bowel must be removed, the distal section being not nearer than  $2\frac{1}{2}$  inches from the anal sphincter, are usually best removed through the Kraske sacral incision, with resection of the coccyx and part of the lower sacrum. In such operations the following procedure may be instituted: (1) A freely mobilized bowel projecting through the anus may, at times, be sutured outside; (2) a large tube may be sutured within the bowel with the terminus just within the anus; (3) a sacral anus may be made and the anal segment sacrificed; (4) a permanent colostomy may be made and the whole rectum removed at the same time or at a later period. A permanent colostomy, however, is quite abhorrent to all patients, and, if it is possible, they much prefer to have the intestinal delivery near its normal location, even if uncontrolled, and at some additional risk from recurrence of the disease. There is no question but that the efforts to restore function or near function in cancer of the rectum and the efforts to obtain good cosmetic results in external cancer have added much to the high percentage of recurrence following operative procedures. Permanent colostomy with total extirpation of the rectum undoubtedly gives a higher percentage of cures than do the methods which restore function.

In patients suffering from cancer of the rectum in the region described we advise a colostomy, and through the incision made for this purpose the hand should be inserted and a general examination made of the abdomen, as well as of the pelvis. If metastasis has occurred, precluding cure, or if impending obstruction demands it, a permanent colostomy is made. If there are no contraindications because of metastases, a temporary colostomy is made with a sufficient spur to deflect all the fecal flow through it.

The upper sigmoid should be elevated so that the lower sigmoid need not be shortened so as to prevent the loosening of enough of it to bring together the anterior and posterior sections after the removal of the cancer-bearing area. A clear understanding should be had with these patients that, if the extent of the disease found at exploration precludes the possibility of resection with good union, and yet if total extirpation of the rectum should

come within the limits of advisability with cure, a permanent colostomy is to be made, with the preservation of all the colon possible. For this we employ a Gersuny twist through the rectus opening of the delivery portion, or the Littlewood type of colostomy through the lateral heavy oblique muscles. Both give exceedingly good control. In either case, at the end of twelve to fourteen days a total extirpation of the rectum is made through the Kraske route.

In the separation of the carcinomatous bowel from the surrounding tissues great care is exercised to prevent opening it and contaminating the wound. After the pelvic peritoneum is opened the upper rectum and lower sigmoid can easily be drawn down to a great extent, and when sufficiently loosened the peritoneal opening is closed by reattaching its parietal layer to the sigmoid at a higher level with catgut sutures.

Upon completion of the division of the intestine, cutting between two pairs of forceps applied above and below the growth, the slightly exposed surface of the bowel is cauterized by the hot iron to sterilize it and effectually sear the surface against grafting thereon any loose cancer-cells that may be within the intestine.

While  $2\frac{1}{2}$  inches of the terminal rectum is usually the limit of preservation with function of the sphincter, 4 inches is much more convenient in resuturing the intestine. The lower segment is usually nearly twice the diameter of the upper or sigmoidal portion. About three-quarters of the circumference is surrounded by peritoneum. This smaller upper end of the bowel is now split on the surface anterior to its mesentery, the incision extending up the bowel for  $1\frac{1}{4}$  inches, thereby adding  $2\frac{1}{2}$  inches to its circumference. Upon cutting the sharp points from the divided edges the circumference becomes as great at this point as at the distal fragment. Since it is desirable to have the diameter of each end alike for a continuous suture, it may be advisable to make two shorter incisions on either side of the bowel. This extra size is demanded because the suture reduces the lumen by nearly one-half. While there is no peritoneum covering the lower segment of bowel at the point of suture, it is well known that a peritoneal surface is required only on one side for rapid healing.

To avoid fistula in the suture line, which would usually occur at the free peritoneal or mesenteric side of the upper segment, the

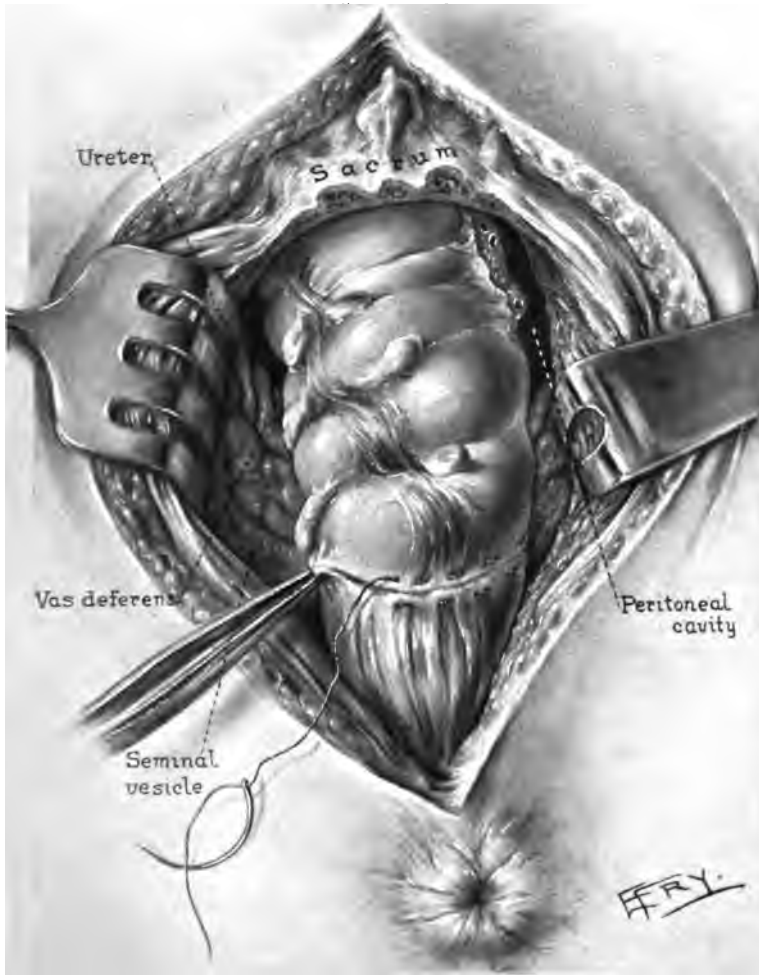


Fig. 118.—Rotation of bowel to protect the mesenteric area.

bowel is rotated one-half to bring the peritoneal surface posteriorly. This protects the mesenteric border. For the through and through suture, inverting the mucosa, chromic catgut is used, and this is

supported by sutures of fine silk which form a second row. At this stage two or three ounces of melted vaselin are poured over and into the cavity of the wound, especially the upper portion, where the parietal peritoneum has been closed. A few sutures bring the structures together loosely over the area of sutured bowel. A rubber tissue drain is inserted on either side of the intestine, and brought out of the sacral incision. If the anus is not relaxed, it is divulsed. If it shows any contraction upon examination, it is well to divide the sphincter muscle anteriorly. This soon heals, but permits thorough drainage temporarily from within the intestine. The rather large cavity which is apparent during the process of the work is quickly filled by intra-abdominal pressure as soon as the position of the patient is changed from the operative one of abdominal recumbency—legs flexed at hips over the table. Without fecal discharge there is very little danger of fistula, but should one occur, it is usually so tortuous that it closes itself. The colostomy incision can be closed, as a rule, two weeks after the resection of bowel.

For the treatment of cancer higher up there are several methods of extirpation, with or without union, all depending on the extent and conditions in the individual case. When situated lower, the sphincter must, of course, be sacrificed.

#### SUMMARY

1. The method permits thorough abdominal exploration.
2. A primary or permanent colostomy should be made in the majority of cases of this type.
3. Increasing the lumen of the anterior and, if necessary, of the posterior portion of the bowel to double their diameter.
4. Rotation of the anterior bowel covered with peritoneum to secure the rapid healing posteriorly.
5. Stretching or division of the sphincter to secure drainage of the bowel.
6. Closure of the colostomy to secure function.
7. If colostomy is permanent, remove rectum at second operation.



## **URINOGENITAL ORGANS**



## INFECTIONS OF THE RENAL PELVIS AND URETER\*

WILLIAM F. BRAASCH

Infection of the renal pelvis necessarily occurs together with infection in the adjacent renal tissue and in the ureter and bladder. Although such a process would, to be exact, be termed a pyelonephro-uretero-cystitis, we are accustomed to refer to the infection as that portion of the urinary tract which is most extensively involved. For example, if the infection is localized largely to the pelvis, it is termed "pyelitis." In this paper the discussion of the condition will be limited to those cases in which the active infection is confined largely to the pelvis, and not to such as are secondary in degree to that in the renal parenchyma.

The trend of recent observation is toward the theory that pyelitis is usually a descending infection from the kidney or part of a pyelonephritis. That renal infection is carried by the bloodstream as a result of lowered resistance of the tissue is the opinion generally held. Another avenue of infection is suggested by those observers who believe that it arises from the bladder and is carried to the substance of the kidney either by the lymphatic supply connecting the bladder with the pelvis or by direct extension.

Cases of pyelitis may be divided into two groups: (1) Those evidently caused by mechanical obstruction to the urinary tract, and (2) those having no evident predisposing factor. Taking for consideration the latter group, we find that, among 164 cases observed in the Mayo Clinic during the past five years, 112, or 68 per cent., occurred in the male, and but 52, or 32 per cent., in

\* Read before the Texas State Med. Soc., San Antonio, May 7, 1913. Reprinted from the Texas State Journal, vol. x, 1914.

the female. The preponderance of infection in the male is difficult to explain. While it is true that pyelitis is frequently found in males who have previously had gonorrhea, a large number deny venereal infection and show no evidence of having had it. It would seem that the same factors, probably anatomic, which cause a preponderance of renal tuberculosis in the male predispose them to other renal infections.

Among the 164 cases regarded as pyelitis, pus was found in the urine of both kidneys obtained by ureteral catheterization in but 131. This does not indicate, however, that the other cases were unilateral. Bilateral pyelonephritis may be present with the following findings:

1. With pus in the catheterized specimen from both ureters.
2. With pus present in one ureter and negative urine microscopically or occasional leukocytes in the other.
3. With microscopically negative urine or occasional leukocytes from both ureters.
4. With urine microscopically negative from both ureters, but cultures from one or both showing bacterial infection.
5. With urine negative microscopically and on culture from both ureters, but showing evidence of previous infection by the pyelogram.

In other words, with pyelonephritis the infection may be temporarily inactive on one or both sides, as evidenced by the absence of pus and bacteria in the catheterized urine. The cicatricial changes in the renal pelvis and ureter subsequent to previous infection can usually be demonstrated in the pyelo-ureterogram, and may be the only positive evidence of bilateral infection. Although pus may be absent from one or both ureters, not infrequently cultures from the urine catheterized from the ureter under aseptic precautions will show the presence of an infecting organism which will be the cause of probable subsequent acute exacerbations. An absence of pus, therefore, after a course of treatment would not necessarily indicate a permanent cure. In many cases the infection becomes active at irregular intervals, and the absence of pus may indicate that the process is temporarily dormant. The

percentage of patients in whom pyelitis is unilateral will be found to be comparatively small if all the methods of diagnosis are used.

*Relation to Cystitis.*—Practically every case of pyelitis is accompanied by more or less cystitis. Although not every case of cystitis is accompanied by pyelitis, the majority of cases of cystitis will be found to be the result of renal infection. Particularly is this true in the male, where, with the exception of those infections localized to the base of the bladder extending from a urethritis or resulting from local irritation, urinary obstruction, or trophic disturbance, a pyelitis may be demonstrated in practically every case. Thus in 121 cases of cystitis occurring in the male, excluding the aforementioned conditions, evidence of past or present renal infection was found in 109, or 90 per cent. In the female, however, cystitis will be found much more frequently without any demonstrable renal involvement, particularly that chronic type of cystitis so frequently found and which is characterized by mild chronic inflammation of the trigone often occurring in scattered areas and accompanied by more acute subjective symptoms than the organic changes would warrant. However, when the bladder is extensively involved, renal infection may be demonstrated in the majority if not in all cases. It is frequently remarkable how little the bladder may be infected when considerable long-standing infection occurs in the kidney and purulent urine is found coming from both ureters. On the other hand, not infrequently the cystitis may be very severe, and but a few pus-cells be demonstrated in the urine obtained by ureteral catheterization.

*Mechanical Obstruction.*—Pyelitis resulting from mechanical obstruction to the urine should be considered as quite a different subject. While it is possible that the obstruction to renal drainage may lower the resistance of the kidney and so make it subject to hematogenous infection as in the other group, the conditions are quite distinct. As a rule, when mechanical obstruction is removed, the pyelitis will disappear unless considerable infection and destruction of the substance of the kidney have taken place. In the male such infections result more commonly following hypertrophy of the prostate and with stricture of the urethra. In cases

of long standing the parenchyma may become involved, and the resulting nephritis may become a fatal complication either following operation or without operation. In the female the form of mechanical pyelitis most frequently seen is that accompanying pregnancy. As a rule, the infection is confined more largely to the pelvis than is the case of urinary obstruction in the male, and it usually clears up spontaneously or with the aid of urinary anti-septics. Occasionally, however, the process becomes chronic and extends well into the renal substance, with destruction of vessels and tissue to a varying degree. With pyelitis obstruction to the ureteral catheter is not infrequently met with at the ureteral meatus. In 112 cases of pyelitis in the male such obstruction was noted on both sides in 26 cases and on one side in 8; whereas in 42 cases occurring in the female it was noted on one side in 4 cases and on both sides in 1. Such obstruction is to be regarded as the *result* of the inflammatory process in the ureter and bladder and not as its cause. It is usually found in cases where the inflammation of the bladder is marked, and is probably the result of the edema and congestion in the wall of the bladder.

*Subjective Symptoms.*—Pyelitis is not usually the cause of severe pain. Frequently the patient may complain of an occasional dull ache referred across the sacral or lumbar area. When, however, the process has advanced so far as to cause mechanical obstruction to the urine, attacks of severe pain usually follow. Pain may be the result of mechanical obstruction to the urinary secretion, increase in intrarenal tension resulting from diffuse cortical infection or perinephritic infection. The causes for mechanical obstruction are: (1) Cicatricial changes subsequent to peripelvic infection; and (2) occluding blood-clots subsequent to bleeding, such as occurs with pyelitis granulosa. With a considerable degree of infection in the peripelvic tissues the pelvis and pedicle of the kidney are often found firmly bound down with dense adhesions. This process may also involve the adjacent ureter, and cause considerable distention of the ureter and pelvis. The upper ureter and pelvis are then seen dilated partially by peri-ureteral and peripelvic adhesions and partially by mechanical obstruction. Oc-

casionally with long-standing pyelitis the patient complains of spells of dull, persistent pain, with varying degrees of temperature and malaise, occurring at irregular intervals. This can be explained best by sporadic acute infection of the adjacent renal parenchyma, with subsequent increase of intracapsular tension.

*Pyelographic Data.*—While radiographic data and the cystoscopic examination are of value in the diagnosis of pyelitis, they may be insufficient in ascertaining the degree of renal destruction and in determining whether or not the condition be surgical. This is best ascertained by pyelography.

The outline of the pelvis in pyelonephritis as seen in the pyelogram may show any of the following abnormalities: (1) Dilatation of the individual calices, with little or no pelvic dilatation. (2) Dilatation of the renal pelvis, with little or no dilatation of the calices. (3) Dilatation of both calices and the pelvis. (4) Narrowing of calices and pelvis, with dilatation of the ureter, particularly the first part. Where the dilatation of the calices is predominant, the pyelitis is often the result of local infection, as from stone. In such cases the pelvis may be seen to be but slightly enlarged, with considerable irregular dilatation of the calices. Occasionally, with a small stone lodged in a calyx, this calyx alone is seen dilated, even to a considerable degree, while the remaining calices may show little or no change. Dilatation of calices is also seen predominant with certain types of chronic pyelonephritis when the infection is largely in the renal parenchyma. Dilatation of the pelvis, with little or no dilatation of the calices, may be seen in that type of pyelitis where the infectious process is confined largely to the pelvis, and particularly in its early stages. Unless the calices are fully distended while making the pyelogram, this type may be misinterpreted. The typical dilatation of pyelitis, however, is one where both the pelvis and calices are seen irregularly dilated to a varying degree. The outline may be distinguished from that of early hydronephrosis in that the calices are usually narrower at the base, where they leave the pelvis, whereas their ends are relatively larger and more irregularly rounded. With extension of the inflammatory process and destruction of the adjacent renal

parenchyma the dilatation of the pelvis and calices may become considerable and assume the proportions of a pyonephrosis. Where the infectious process is chronic and predominant in the substance of the kidney, the outline of the pelvis and calices may appear narrowed and unusually small. The calices may appear as narrow streaks radiating from the true pelvis. In such cases the ureter will be found dilated, particularly in its upper part, to a considerable degree. In fact, the dilated ureter may often be the only pyelographic evidence of the inflammatory process. The inflammatory dilatation of pelvis and ureter usually remains to some extent even after the active infection has ceased, and remains as indelible evidence of previous infection. In general, the outline of this inflammatory distention may be differentiated from that caused by mechanical obstruction by its irregularity, and by the fact that the changes are confined largely to the calices, the free pelvic wall becoming distended only when the process is extensive. When ureteral obstruction later on complicates a pyelitis, the pelvic outline may show the characteristics of both mechanical and inflammatory distention.

#### DIFFERENTIAL DIAGNOSIS

*Unilateral renal tuberculosis* may occasionally be confused with a unilateral pyelitis unless a careful search for tubercle bacilli and a guinea-pig inoculation is made. Not infrequently the delay and technical difficulties accompanying guinea-pig inoculation, however, make more rapid diagnostic methods desirable. The absence of tubercle bacilli in the microscopic examination of the urinary sediment would not necessarily exclude tuberculosis. Although the cystoscopic examination may show changes in the bladder which are typical of tuberculosis, we occasionally find a unilateral pyelitis, with ulceration and inflammation of the mucosa of the bladder, which cannot be differentiated from that accompanying renal tuberculosis. Furthermore, both conditions may cause little or no inflammatory change in the mucosa of the bladder, so that the absence of ulceration is diagnostic of neither. Multiple strictures of the ureter, when found, usually accompany



tuberculosis. As I have previously described, pyelography may be of considerable value in differentiating between pyelitis and renal tuberculosis. Although the outline of the pelvis with pyelitis becomes irregularly dilated to a varying degree, as shown in the pyelogram, nevertheless it is usually well defined. With advanced renal tuberculosis and surgical pyelitis or pyonephrosis, however, the outline of the pelvis is often indefinite, and may be seen to be connected with a cortical abscess. With an early tuberculosis, however, no cortical abscess may be visible, and the pelvic changes will resemble those of a pyelitis. Pyelography is, however, not to be employed when the diagnosis can be made from the cystoscopic and clinical evidence, since the colloidal silver may occasionally cause irritation when it does not drain out of the cortical and pelvic cavities.

A clinical differentiation between the comparative degree of infection in the pelvis and parenchyma may be difficult. The clinical picture of acute septic nephritis is usually easily recognized. A chronic infectious process, however, involving the parenchyma primarily and the pelvis secondarily, may be accompanied by the same lack of subjective symptoms, other than urinary, as occurs with typical pyelitis. As a rule, with nephritis the urine is less purulent, and may even have at times an occasional pus-cell. In the pyelogram the pelvic dilatation is usually but slight, while infection is predominant in the parenchyma. Again, the urine from a pyelitis may appear on cystoscopic inspection to be so purulent as to lead one to believe that the kidney is largely destroyed. On exploration one is frequently surprised at the moderate changes apparent in the pelvis and the slight evidence of parenchymatous infection.

A radiogram should be made as a routine procedure whenever a catheterized specimen of the urine shows pus, since renal stone may be the cause of pus in the urine without producing any pain. In 250 cases of renal stone operated on in the Mayo Clinic no definite pain was given in 24 cases, or 10 per cent. The stone may be either the primary cause of the accompanying pyelitis or

it may be secondary to pyonephrotic changes of an advanced pyelitis.

It should be borne in mind that gastric symptoms may be reflex from lesions of the kidney, as from disease of the gall-bladder and appendix, although possibly not so often. With pyelitis, particularly if well advanced and of long standing, epigastric distress and gastric symptoms are not infrequently the major and only complaints. Only a routine analysis of the urine will call our attention to a possible pyelitis. It should be remembered, however, that the patient may have two lesions, as well as one; a coincident infection in the gall-bladder or appendix as well as in the kidney is not infrequent.

*Ureteritis.*—Infection in the ureter is usually secondary to an adjacent inflammatory process, and as such can rarely be considered as a clinical entity. Ureteritis may be classified in accordance with the avenue of infection as descending, ascending, and localized. When the entire ureter is found involved, the infection is practically always descending from the original pyelonephritis. When ureteritis is confined to a part of the ureter, it is usually involved in the inflammatory process of surrounding tissue. This may occur with a contiguous appendicitis, pelvic inflammation, vesiculitis, or cystitis. Microscopic blood and pus-cells found in the urine of patients suffering from appendicitis are usually caused by transitional ureteritis, which disappears on removing the cause. While ureteritis involving the entire ureter is probably rarely if ever ascending, it may be partially so, as evidenced by the localized ureteritis frequently found with marked chronic cystitis. The course of the inflammatory process can best be demonstrated in the ureterogram. The portion of the ureter situated in the wall of the bladder is seen markedly dilated where it passes through the bladder and gradually becomes normal in outline at a varying distance above. Even with extensive ascending ureteritis, the process is rarely seen to extend up above the first point of narrowing below the ureteropelvic juncture. The dilatation resulting from ascending ureteritis can occasionally be easily demonstrated by filling the bladder with colloidal silver solution,

lowering the area of the kidney, allowing the fluid to gravitate up the distended ureter, and then making the radiogram. Cystoscopic examination may show the ureteral meatus gaping and the bladder portion of the ureter dilated, as evidenced by the cloudy bladder fluid which flows in and out with respiration. This condition may be particularly misleading in cases of tuberculous cystitis when the kidney on that side is normal.

Another type of ureteritis which may be considered as ascending is that resulting from residual urine in the bladder consequent to prostatic hypertrophy and stricture of the urethra. Although with extreme distention of the bladder the residual urine may back up in the ureter and distend it and the pelvis, all cases of ureteral dilatation accompanying hypertrophy of the prostate cannot be so explained. Not infrequently with but a few ounces of residual urine the pelvis and ureter of one or both sides are found to be thickened and dilated to a considerable degree. The bladder in such cases is usually markedly inflamed, and the urine coming from the dilated ureter is purulent. It is quite evident that the amount of residual urine would be too small to dilate the ureter, although it might have been an etiologic factor in causing the renal infection. In other words, the ureteral dilatation frequently found in patients suffering from hypertrophy of the prostate is more often the result of ureteral infection and not of mechanical distention.

*Pathology of the Inflamed Pelvis and Ureter.*—Whenever the renal pelvis or ureter becomes inflamed, a change takes place in the wall which causes dilatation. With long-standing infection the pelvis and ureter may become several times their normal size. On cross-section of the ureter the walls are seen to be hypertrophied and the lumen is increased in proportion. The pelvis is found to be irregularly enlarged, the calices moderately dilated, and the walls thickened. Microscopic examination shows connective-tissue changes in the walls, with marked loss in elasticity. The degree of dilatation, however, is not so great as that usually seen with mechanical obstruction to the ureter, nor is there such thinning of the walls. Changes in the wall of the ureter are al-

ways present whenever a pyelitis exists. If an acute inflammatory process is confined to the mucosa, no ulceration or stricture results. With tuberculosis and stone erosion the submucosa becomes involved, with consequent stricture. With a moderate degree of infection the changes found in the ureter may be found to be greater than those visible in the pelvis.

*Treatment.*—With *chronic pyelitis* the most important means of treatment at our command are urinary antiseptics, vaccines, and pelvic lavage. In cases of *mechanical pyelitis* removal of the cause is, of course, necessary to effect a cure. Hexamethylenamin alone will seldom be effective in curing a chronic pyelitis, for although in some cases it may ameliorate irritability of the bladder, it may increase it in others.

When the use of vaccines was first advised for chronic pyelitis, much was expected of it. The reports from various observers were at first conflicting. While some still claim that vaccines are of no value, many have found them to be of decided benefit in at least a small percentage of cases. It would be difficult to say from 76 cases of pyelitis that we have treated with vaccines in the Mayo Clinic what percentage of cures should be attributed to the vaccines alone, since pelvic lavage was also employed in most of the cases. However, those cases in which vaccine was employed improved more quickly than when it was not used. The autogenous vaccine is to be preferred.

While it would seem unreasonable to expect irrigation of the renopelvic mucosa to have much curative effect on infection in the deeper tissues about it, experience has proved that such is often the case. Solutions of silver have proved to be the medium of greatest value, according to most observers. Silver nitrate, commencing with solutions of about 1:10,000 and gradually increasing to 1 or 2 per cent., without causing local irritation, has been of the greatest value in my experience. Colloidal silver is also of value, particularly at the onset of treatment. Aluminum acetate, as advanced by Koll, has not been found to be more effective in the 21 cases where it has been employed than silver nitrate, and has the disadvantage of frequently causing considerable local irrita-

tion. Renal lavage should, of course, be carried out only by those expert in the use of the cystoscope and ureteral catheter. In order to obtain the best results it should be given once a week for a period of six to eight weeks, and then possibly every month or two for an indefinite period. The improvement, not alone in the appearance of the urine, but in the general health of many of the patients after lavage of the pelvis, is often remarkable, particularly when there is considerable inflammatory dilatation. In order, therefore, to obtain the best results in the treatment of chronic pyelitis it is best to use all three methods in conjunction, namely, urinary antiseptics, autogenous vaccines, and renal lavage.

Although pyelitis is not usually regarded as amenable to surgical treatment, it occasionally becomes a distinct surgical condition when certain complications set in. The conditions which render pyelitis surgical are as follows: (1) Persistent unilateral pyelitis causing recurrent attacks of fever and weakness; (2) unilateral hemorrhagic pyelitis; (3) extensive inflammatory distention of the pelvis and destruction of renal tissue on one side, as may be seen with advanced pyelitis; (4) ureteral obstruction as the result of peripelvic and peri-ureteral cicatricial changes causing intermittent colic. When any of these conditions is present, nephrectomy is indicated, even though a moderate degree of infection is found to exist in the other kidney.

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## RECENT PROGRESS IN URETERO-PYELOGRAPHY \*

WILLIAM F. BRAASCH

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Ureteropyelography has of late been severely criticized and even condemned on the grounds that it is a painful and dangerous procedure, and, furthermore, an unnecessary one.

Ureteropyelography has been employed in the Mayo Clinic in the treatment of more than 1000 patients without fatality or permanent injury. While we have occasionally observed patients in whom colic followed examination by this method, we not infrequently observe similar symptoms from ureteral catheterization alone, and we expect more or less colic to follow the use of Kelly's overdistention method.

It has been our experience that severe reaction following pyelography is usually the result of error in technic or lack of care in the selection of cases. The following are some of the technical precautions which should be observed in these cases.

1. Colloidal silver (collargol) crystals should be carefully ground in a mortar when put in solution (10 per cent.) and then filtered, otherwise the undissolved crystals may be deposited on the walls of the pelvis and ureter and act as an irritant.

2. The solution should be carefully warmed before injecting—not boiled, since it coagulates with boiling.

3. The solution should be injected by the gravity method (Baker, Stanton, Thomas), watching the patient for the slightest evidence of pain. From 2 to 8 c.c. will usually suffice unless symptoms of obstruction have been previously noted.

\* Reprinted from the Journal of the Michigan State Society, April, 1913, pp. 189-191.

4. A large ureteral catheter should be used so that the injected solution may drain away easily.

5. The apparatus for the *x*-ray and the injection should be so arranged that there will be no delay after the catheter is inserted.

In selecting cases suitable for pyelography it should be remembered that the method is not to be employed unless the existence or nature of a lesion in the urinary tract cannot be diagnosed in any other way. Unless the procedure is strongly indicated the hypersensitive and neurotic individual should not be examined by means of ureteropyelography. Instances have been reported in which deposits of silver with surrounding foci of evident suppuration were found in the cortex of a kidney, which was removed following pyelography. Three similar cases have been observed in the Mayo Clinic, all of which were associated with large hydronephrotic kidneys which did not drain the injected solution. Pyelography is distinctly contraindicated in such cases, and the procedure is not usually necessary in making the diagnosis. It must be remembered, moreover, that merely passing a catheter into a distended renal pelvis with a constricted outlet may suffice to cause similar pain and cortical infections. Severe colic resulted in two patients under my observation who had large hydronephrotic kidneys and in whom Kelly's overdistention method was employed to ascertain the capacity of the kidneys. At operation both kidneys showed cortical areas colored with the methylene-blue used in the distending solution. It is quite evident, therefore, that whenever the renal pelvis cannot drain itself following catheter trauma to the etiologic ureteral constriction, it may force some of the retained pelvic contents up the dilated tubules into the renal parenchyma.

In recent literature our attention is again called to the subject of ureteral kinks and anomalous positions of the ureter as the cause of pain accompanying movable kidney. Schmidt and Kretschmer have shown how variable may be the course of the normal ureter. Fowler claims if a pyelogram is made with the patient first in the dorsal and then in the erect position and the ureter is seen to bend sharply at a fixed point in the pyelogram

taken in the erect position, that we have a ureteral kink and a condition which requires operation. In a series of 12 patients who had no abdominal pain whatever and in whom a movable kidney was accidentally discovered in routine clinical examination in our clinic, an evident ureteral kink was demonstrable in 5 instances in the pyelogram taken in the erect position.

Cabot maintains that the relation of the upper ureter, as it leaves the pelvis, is of value in the diagnosis of early hydronephrosis. While it is true that with hydronephrosis we frequently find the ureter leaving the pelvis at unusual angles and then follow a circuitous or tortuous course, nevertheless, in observing a series of normal pelvises, we often find evident anomalous insertion of the ureter. Whereas at operation we may occasionally find early hydronephrosis, when no pelvic distention could be definitely demonstrated with our present methods of examination, it is difficult to conceive of any long-standing actual ureteral obstruction failing to cause demonstrable dilatation of the pelvis and ureter. In other words, unless the pyelogram shows dilatation of the pelvis and ureter above an evident kink or anomalous insertion, we have no objective indication for operation.

While pyelography has proved to be of value, particularly in the diagnosis of small, early hydronephrosis (Cabot, Braasch) (20 to 30 c.c.), yet it has its limitations. The normal renopelvic outline varies to such an extent that it is difficult to fix the normal limits. The first evidence of previous mechanical retention in the renal pelvis is shown by the broadening of the entire calyx and flattening of its terminal irregularities. Not infrequently, however, the normal pelvis will show evident broadening of several calices and an exceptionally large pelvic outline, which may be difficult to differentiate from the changes of early hydronephrosis. To be of practical value, therefore, the pelvic deformity must be quite marked. Unless the pelvis is fully distended with the injected solution, moderate pelvic distention will be overlooked. This often involves technical difficulties. When a small hydronephrosis is suspected, it is best to use as large a catheter as possible to prevent the return flow of the injected material.



It may be difficult to demonstrate ureteral distention in the radiogram following the injection. Unless the ureter is fully distended, the dilatation may not be apparent and the partially collapsed ureter may appear to be of normal size. When evidence of possible ureteral distention is obtained by means of the catheter, namely, residual urine and obstruction, better outlines may often be obtained by rapidly injecting the colloidal silver with a syringe rather than by the gravity method. Ureteral dilatation resulting from infection and without constriction may be difficult to show unless a catheter be used large enough at least partially to prevent the return flow of the injected medium. The outline of the normal ureter may occasionally appear abnormally large because of the considerable amount of return flow, but the apparent distention can usually be differentiated from a slight abnormal distention, since the broadening caused by the return flow is evident only in areas giving an irregular outline to the ureter. The possibility of demonstrating distention of the ureter by means of permitting the colloidal silver solution to run into the ureter from the injected bladder with the patient in the Trendelenburg position has been advocated by various observers (Uhle), but has not proved to be of practical value, except in a few cases in which the ureteral dilatation involved the meatus. The meatus is not, as a rule, found dilated with ureteral dilatation except with ascending infections accompanied by severe cystitis or with extreme bladder retention of long standing.

The use of gas as a medium instead of colloidal silver has been advanced by different observers. Cole advocated the injection of air, and more recently Lichtenberg suggested the use of oxygen. Theoretically, either air or oxygen should be an admirable substitute and would obviate the disagreeable features of the colloidal silver. Simplicity of technic in making the injection, absence of after-pain, rapid drainage, and the advantages gained in localizing the renal stone are all arguments in favor of gas. In our experience, however, the use of gas with the present technic or method of application has not been practical. The first obstacle encountered, in spite of careful preparation, is the diffi-

culty of eliminating gas in the bowel. The confusion of the shadow in the renal pelvis with the shadow caused by the gas in the adjoining bowel renders interpretation uncertain. Furthermore, in the majority of cases it is difficult to keep the pelvis fully distended while the radiogram is being made. The consequent lack of detail in the air-distended outline is a distinct disadvantage. It is usually impossible to distend the ureter with gas, and at best the procedure is uncertain.

The clinician who has had considerable experience with cystoscopy and with the interpretation of shadows in radiograms of the urinary tract, and who has an opportunity to see his diagnoses checked up at the operating-table, realizes that these diagnostic methods will frequently mislead the operator. Naturally, the more experienced the clinician, the less will be the percentage of errors. But even with wide experience the two diagnostic methods, when used independently, often fail in the diagnosis of hydronephrosis, the identification and extent of inflammatory changes in the kidney and ureter, differentiation of extrarenal and extra-ureteral shadows, localization of renal shadows, identification of renal tumors, identification and localization of ureteral obstruction, hydro-ureter, and of congenital anomalies. It is in the above conditions that ureteropyelography alone can give us accurate data as to the nature and extent of the lesion. Whether or not this will be regarded as necessary depends on the degree of accuracy desired in the diagnosis.

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## CLINICAL OBSERVATIONS ON ESSENTIAL HEMATURIA\*

WILLIAM F. BRAASCH

For want of a more accurate term, I have retained that of "essential" for the type of hematuria which has not as yet been explained by any of the definitely established renal conditions causing hemorrhagic urine. The term "essential" should be limited to those cases of hematuria showing neither clinical evidence of renal insufficiency, visible organic change in the renal parenchyma, nor renal infection. The operative records of the Mayo Clinic up to June 1, 1913, show that 26 patients were operated on for renal hematuria for which no evident cause could be found. The clinical records show 51 patients not operated on in which the clinical diagnosis of essential hematuria was evident.

### SYMPTOMATOLOGY

*Sex.*—Of the 77 patients, 58, or 75 per cent., were males and 19, or 25 per cent., females. The preponderance of males is noteworthy and is in keeping with that of renal infection occurring in the male.

*Age.*—At the time of examination 6 patients were under thirty years, 10 between thirty and forty, 24 between forty and fifty, 17 between fifty and sixty, and 12 over sixty. The majority of cases occurred in persons between the ages of forty and fifty, while only a small number of patients were below thirty years.

*Localization.*—On cystoscopic examination the disease was

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localized to the right side in 51 cases and to the left side in 26. Pain was described as a dull ache across the sacrum in 10 of the 77 cases, in either lateral abdomen in 6 cases, but never to such a degree as to be of any practical significance. It was described as severe in 5 cases, and then only with hematuria, the pain evidently being caused by blood-clots blocking the affected ureter.

*Duration of Symptoms.*—Of the 26 patients operated on, hematuria had first appeared over a year before in 16, or 61 per cent., over five years in 10 cases, or 38 per cent., and fifteen years or more in 5 cases, or 19 per cent. It had continued prior to operation for a year or more in 5 cases, or 19 per cent., over three months in 18, or 69 per cent., and over a month in all but 3 of the cases. Of the 51 patients not operated on, hematuria was noted less than three months before in 23 cases, over a year before in 12, or 23 per cent., over five years in 10, or 19 per cent., and over ten years in 5, or 9 per cent.

*Physical Findings.*—In 3 of the cases the affected kidneys appeared to be enlarged, on palpation, as though there might be tumor, but at operation they were found to be large, normal kidneys. In 3 other cases the kidney was described as low-lying and movable, in 2 of which the condition was found bilateral. Evidence of a central nervous lesion or marked neurosis was absent in all. In the 34 cases in which the blood-pressure was recorded the average was 132; in 2 cases it was more than 150. Ophthalmoscopic findings were practically negative in all. The general strength was lowered to such a degree that 19 of the 26 patients operated on and 6 of the 51 patients not operated on were unable to carry on their daily occupation. The average hemoglobin estimate of the patients operated on was 63 per cent., while that of the patients not operated on was 84 per cent.

*Urinalysis.*—The specific gravity of twenty-four-hour specimens taken in 21 of the cases in which there was operation was below 1.015 in but 3 cases. In the other cases the average was 1.023. Albumin in varying amounts was found in all the cases in which operation was performed, as was to be expected as a result of the hematuria present at the time of examination. A few hyaline

casts were found in 4 cases and occasional granular casts in 2 cases. A few microscopic pus-cells were found in 5 of the cases in which the patients were not operated on.

*Hematuria.*—The hematuria was reported as being present in a marked degree in 54 cases, or 70 per cent., and but slightly in 23 cases, or 30 per cent. In 63 cases it varied in degree at various times.

*Pyelogram.*—The pyelogram with essential hematuria necessarily shows the outline of a normal pelvis. Evidence of abnormality would call our attention to the probability of some other condition being present, even though no other symptoms were found.

#### DIFFERENTIAL DIAGNOSIS

The diagnosis of essential hematuria is most often confused with that of chronic nephritis, infectious nephritis, pyelitis, neoplasm, tuberculosis, and lithiasis.

*Chronic Nephritis.*—The hematuria of nephritis is sharply defined from that of essential hematuria. It is usually present in a lesser degree and may vary from day to day. Scanty urine and the presence of many granular casts, edema, headache, increased arterial tension, lesions in the retina, any or all of which characterize nephritis, are necessarily absent with essential hematuria. Borderline cases which may have some characteristics of both conditions rarely occur. The conditions are usually widely separated clinically and it is difficult to understand from a clinical point of view how any relationship can be traced between the two conditions. When hematuria occurs with chronic nephritis, it is usually regarded as a terminal symptom, whereas it may be disregarded in a case of proved essential hematuria.

*Infectious Nephritis.*—Chronic infection in the kidney may be the cause of hematuria often resembling that of essential hematuria. It may appear insidiously without clinical evidence of infection other than microscopic pus and bacteria in the urine. More often, however, it is characterized by attacks of dull pain referred to one or both kidneys, chills and fever, together with microscopic pus,

bacteria, and gross hematuria. The hematuria is usually slight or comparatively moderate in degree. It may be present only during the acute attack or it may appear irregularly without the clinical evidence of infection. Pain, which is usually slight with essential hematuria, may be marked with the infectious nephritis, and is more often accompanied with fever and chills and other evidence of infection. The infecting organism can usually be identified in the urine taken under aseptic precautions. As Billings has reported, the hematuria and other symptoms may disappear on administering autogenous vaccine. This was the result in one of four cases in which the vaccine was tried in our clinic. The clinical evidence of renal insufficiency is usually absent until late in the disease. Although this condition is more often bilateral, four patients have been operated on in whom the clinical findings and subsequent course would indicate that the infection was unilateral. In these cases the kidney was found at operation to be smaller than normal, soft and irregular in contour. On section cicatricial changes of evident previous infection were apparent. Needless to say, with essential hematuria the urine should be free from pus and bacteria. The cicatricial changes in the pelvic outline of infectious nephritis as shown in the pyelogram are not usually extensive enough to be of diagnostic significance.

*Bleeding Pyelitis.*—Hematuria is occasionally present with chronic infection of the renal pelvis. It occurs with a chronic indolent infection confined largely to the pelvis and without much active destruction of the substance of the kidney. The infective process may involve the tissues about the renal pelvis and the adjacent ureter to a varying degree. Subsequent cicatricial contraction and adhesions will bind the pelvis and renal pedicle firmly and distort the pelvic lumen. When the upper ureter is involved, it may either become dilated or partially constricted as a result of the cicatricial process. The mucosa of the pelvis in such cases shows irregular areas of inflammation and congestion which bleed on touching, and on close inspection appear to be granular. Between these areas the mucosa may be seen pale and glistening as

the result of the chronic cicatricial changes. On microscopic examination the granular mucosa shows a papillomatous proliferation of cells. The latter condition was first described by H. Chiari and recently by von Frisch, and is called pyelitis granulosa. Occasionally the papillæ alone are involved and the hematuria may result from the consequent papillitis. The hematuria which is seen occasionally with extensive hydronephrosis is caused by a similar condition in the mucosa, as the evident result of a chronic indolent infection. Clinically, hematuria of pyelitis may be subjectively differentiated from the essential hematuria by the character of the pain which frequently accompanies pyelitis. It is usually a dull, persistent pain, with irregular acute exacerbations occurring without evident cause. Pain with essential hematuria is exceptional and occurs only as the result of an occluding blood-clot. Bleeding pyelitis might be confused with that of infectious nephritis, which, however, occurs more often in typical attacks with chills, fever, and slight hematuria. On urinalysis microscopic pus will always be found with pyelitis granulosa. Because of the indolent type of the infection but a few pus-cells may be present among the red blood-cells. Needless to say, only the specimen obtained by ureteral catheterization is of value, because pus-cells in the voided urine may come from any extrarenal source. The most accurate method of differential diagnosis is obtained through pyelography. The outline of the pelvis and adjacent ureter will appear irregularly narrowed and dilated. One or more of the calices may be irregularly dilated; more often they are effaced.

*Neoplasm.*—Although the hematuria of neoplasms is often present to a marked degree, like that of essential hematuria, it usually persists but a short time and appears at irregular intervals. Unfortunately, the occasional short hemorrhage does not cause the average patient to consult a physician so often as the protracted one. The presence of tumor will usually identify the nature of the hematuria, but in 12 of 91 patients operated on for malignant tumor of the kidney at the Mayo Clinic definite tumor could not be determined clinically. It is this group of tumors which is

easily confused with essential hematuria. Two methods are available in identifying the existence of a surgical condition, namely, pyelography and the renal functional estimate. It has been shown that the kidney with essential hematuria will not manifest any marked decrease in functional activity as measured by the secretion of phenolsulphonephthalein injected. It has been my experience that non-infected neoplasms without hematuria will show decrease in function in but 25 per cent. of cases. Unfortunately, renal tumors too small for definite palpation would show even a smaller percentage. Furthermore, profuse hemorrhage offers considerable technical difficulty in the accurate estimation of the amount of dye secreted. With marked comparative reduction of functional activity of the bleeding kidney, however, the existence of neoplasm should be suspected. Pyelography will more often be of value in ascertaining the existence of neoplasm by demonstrating an abnormal outline of the renal pelvis subsequent to tumor retraction. While recognizable deformity of the pelvis may be demonstrated in over two-thirds of tumors of the kidney that come to operation, early tumor may not show recognizable deformity. Nevertheless, any tumor that is so far advanced as to cause hematuria will probably cause recognizable pelvic deformity. Even after all possible clinical evidence has been obtained, the question will often be raised whether or not operation is indicated. Tumor of the kidney was discovered at operation in two cases in which the clinical evidence rather suggested essential hematuria.

*Renal Tuberculosis.*—Occasionally the first and only evidence of renal tuberculosis is hematuria. In such cases the hematuria will usually be well marked and persist but a day or two, often showing but one hemorrhage. In the absence of pus in the urine and other evidence of tuberculosis on physical and cystoscopic examination, its existence could easily be overlooked. If there is any probability of tuberculosis, guinea-pig inoculation should always be made. Of 3 cases of hematuria regarded on clinical examination as being essential, 2 were proved to be tuberculous



on subsequent examination, and in 1 the patient was reported as having died of renal and pulmonary tuberculosis.

*Lithiasis.*—A small stone pocketed at the end of a calyx may be the cause of an otherwise symptomless hematuria and remain undiscovered even with the most careful roentgenographic technic. Urinalysis will usually show the presence of old blood-cells, but no pus. A careful search should also be made for crystals, particularly those of calcium oxalate, which, if present in a considerable quantity, would be very suggestive of the existence of stone. On exploring in two cases regarded clinically as essential hematuria, such a stone was found at the end of a calyx in one. In the other case a stone 2 cm. in diameter was found in the cortex, which, because of its soft character and the unusual obesity of the patient, did not show in the roentgenogram. Two more patients regarded clinically as having essential hematuria but not operated on reported having passed small stones several months after returning to their homes.

*Renal Varix.*—With the publication of a case showing angioma of the renal papilla Fenwick advanced a new explanation for a certain group of cases which had hitherto been called essential hematuria. It was at first believed that this condition would explain a large proportion of cases of essential hematuria. Recently a number of such cases have been reported in American literature. These might give the impression that the condition is a common one. Any report of such a condition without a microscopic section showing the dilated condition of the papillary blood-vessels cannot be of accurate value. Clamping the pedicle and consequent congestion of the tissue of the kidney may cause the papillæ to appear so engorged as to give an impression of abnormality. True angioma is a comparatively rare condition and can explain but a very small percentage of bleeding kidneys. One such case has come under our observation in which microscopic section showed the typical dilated structure of the blood-vessels. The condition may be readily confused with the varicose condition of the blood-vessels adjacent to the pelvis as the result of insidious infection in the pelvis and surrounding tissues. With infection of the tissues

the veins of the papillæ will occasionally be found dilated on microscopic section. Leukoplakia of the pelvis was discovered on exploring the pelvis of the kidney in a case believed on clinical examination to be bleeding, because of essential hematuria. Pyelography will not, as a rule, be of much value in identifying the changes which affect the pelvic outline but moderately.

*After-course.*—Of the 26 patients operated on, nephrotomy was performed in 12 cases and nephrectomy in 16. Exploration was made in 1 case. In 2 of the 12 patients in whom nephrotomy was made the hematuria persisted to such a degree that nephrectomy was necessary in 1 case three months and the other four months after the first operation. In 1 case hemorrhage through the wound persisted, necessitating nephrectomy two days after nephrotomy. In 1 other case of nephrotomy made four years ago the patient reports occasional hematuria in a diminished degree. The 8 patients reporting recovery following operation were operated on 1 six years, 1 four years, 2 three years, 2 two years, and 2 one year ago. In the patient operated on four years ago hemorrhage was reported occurring a year after operation, but none since then. Of the 16 cases of nephrectomy, 1 patient died elsewhere six months after operation from some unknown cause, and 1 was not heard from. Fourteen patients are living and are reported in excellent health 1 twelve years, 1 eleven years, 3 eight years, 1 nine years, 2 six years, 2 four years, 1 three years, 1 two years, and 3 two years after operation. It will be noted, therefore, that nephrotomy is not to be regarded as a certain method of cure. The fact that recovery followed in 8, or 67 per cent., of the cases, should recommend it, provided the affected kidney appears quite normal on exploration. On the other hand, the excellent results obtained from nephrectomy should recommend such procedure providing the hemorrhage prior to operation had been severe enough to warrant it, that the patient's general condition was otherwise good, and that the functional activity of the other kidney was previously ascertained. Of the 51 cases not operated on, we were able to trace but 44. In 26 of these cases the affected kidney was merely catheterized, with cessation of hematuria following.

This cessation of symptoms remained permanent in but 4 cases. In 18 cases the pelvis was overdistended with methylene-blue or colloidal silver solutions, with permanent cessation of hematuria in but 3 cases. In 6 cases epinephrin (adrenalin chlorid) in solutions of 1 : 2000, as advanced by Young, was introduced into the pelvis of the affected kidney. Recurring hematuria was reported in all cases except one treated six months ago. In one of two cases treated three years ago, hematuria was reported stopped over a period of one and one-half years. Horse-serum was injected in two cases, and human serum, as suggested by Barringer, in one case, with no immediate cessation of symptoms.

*Treatment.*—From the foregoing results it would seem advisable, as a rule, to treat essential hematuria conservatively. Needless to say, every means of diagnosis should be employed before exploration is undertaken. It has been our rule not to advise surgical exploration unless the hematuria was so marked as to incapacitate the patient or whenever evidence existed which suggested the possibility of neoplasm. The question of whether or not to explore for a possible neoplasm is one of the most difficult problems to solve in the clinical examination of hematuria. The possibility of renal tumor in a patient over forty years of age whose general condition is below par and who has no clinical evidence of nephritis would justify surgical exploration even though the hematuria itself were not severe enough to warrant it. Exploration is not justifiable when no clinical evidence exists other than one or two spells of hematuria. In such cases ureteral catheterization or any of the various methods of renal pelvic irritation, such as overdistention, pyelography, epinephrin, etc., should first be tried, or, as has been recently suggested, the injection of blood-serum. An occasional moderate hematuria without other clinical symptoms recurring after these measures have been tried should not necessarily require any form of treatment. When the hematuria has incapacitated the patient, however, or when neoplasm is regarded as possible, exploration is indicated. The good results obtained from nephrotomy would justify its use, provided nothing is found wrong with the kidney on exploration. If, on exploration,

however, any evidence of previous infection or tissue-destruction exists, or if nephrotomy should fail to stop the bleeding, nephrectomy is indicated.

*Etiology.*—Of the various etiologic factors that have been advanced to explain essential hematuria, nephritis seems at present to have the most supporters. Of recent years pathologic evidence in support of this theory has been advanced by Israel, Nichols, Kretschmer, Kapsammer, Stoerk and others. Microscopic examination of bleeding kidneys removed at operation and postmortem discloses areas of greater or lesser extent with varying degrees of nephritis in practically every case if carefully searched for. An examination of the pathologic material of bleeding kidneys removed at the Mayo Clinic shows eleven specimens. Of this number, three show nothing but a few glomeruli with cicatricial changes; one is quite normal on serial section, and the others show moderate degrees of increase of interstitial connective tissue as well as glomerular changes. None of them show the marked destructive changes found with clinical chronic nephritis. Section of kidneys removed in the last 320 post-mortem examinations of patients (Broders) who had no clinical evidences of advanced renal disease, shows some evidence of nephritis in 200 cases, or 63 per cent. In none of these cases had hematuria ever been reported and none had clinical evidence of nephritis. On comparing microscopic sections it was impossible to differentiate the character of the microscopic changes found in the bleeding and non-bleeding kidneys. It is quite evident that there must be some other factor involved which causes one of two kidneys to bleed when the microscopic changes are quite similar. Because nephritic changes are found in a bleeding kidney it does not necessarily follow that nephritis causes the hematuria.

The clinical evidence obtained on examination and observation of the after-course of patients suffering with essential hematuria does not support any nephritic etiology. Four of the patients operated on and three of those not operated on gave histories of hematuria of fifteen years or more prior to examination. If the hematuria were one of the earliest symptoms of nephritis

the progress has been rather slow. Furthermore, the number of patients who have been entirely well five years or more following nephrectomy is not in keeping with the usual course of a patient suffering with chronic nephritis from whom one of two diseased kidneys has been removed. Whatsoever the cause of the hematuria may be, if systemic, it apparently does not tend to shorten life, at least to any great extent. In support of the nephritic theory it has been advanced that many cases show traces of albumin or occasional casts in the urine in the interval when no hematuria is present. The routine examination of the urine of 5000 patients examined consecutively in our clinic during the past year shows trace of albumin in 1450, or 29 per cent. Less than 100 of these patients had any clinical evidence of nephritis and none of them had essential hematuria. The overwhelming proportion of patients with albuminuria as compared with those suffering from hematuria demands further explanation than that of nephritic change. Furthermore, the term "nephritic" is an unfortunate one for this type of hematuria now called "essential," and tends to confuse it with the hematuria accompanying acute and chronic nephritis, which is clinically quite distinct.

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## CLINICAL DATA ON RENAL LITHIASIS \*

WILLIAM F. BRAASCH

The classic symptoms of renal lithiasis, namely, hematuria, and acute pain referred to the area of the kidney with anterior and downward radiation, were found present in but 117, or 46 per cent., of the 251 patients operated on for renal stone at the Mayo Clinic from January 1, 1900, to January 1, 1913. In 30 patients, or 12 per cent. of the total, the pain was referred to the region of the gall-bladder, with posterior radiation suggestive of disease of the gall-bladder. In 32 patients the pain was referred to the lower abdomen, with upward and lateral radiation, suggestive of appendiceal disease. Pain was referred to both sides in 56 patients, or 22 per cent.; largely to the affected side in 40, or 15 per cent., and more to the non-affected side in 16, or 6 per cent. Pain was absent or very slight in 21 patients, or 8 per cent.; and in 26, or 10 per cent., pain was general over the abdomen. Furthermore, it must be remembered that numerous lesions of the kidney other than stone, as well as disease in the perirenal organs, will cause similar localization and radiation of renal pain.

Even more confusing, from a surgical point of view, is the localization of the stone, since in 107 of the 131 cases of stones in the ureter operated on in the Mayo Clinic the pain was referred largely to the area of the kidney, and its radiation was similar to the pain accompanying that of renal stone. It will be seen, therefore, that the subjective localization of pain associated with renal lithiasis is so variable that it offers but few data of exact diagnostic value. In order to exclude lithiasis, it becomes necessary to

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radiograph the abdomen for practically every indefinite pain which is not accompanied by other clinical data to identify it.

*Value of the Radiogram.*—It is well known that a radiographic shadow located in the region of the kidney does not necessarily indicate renal lithiasis. The majority of such shadows can be recognized from their shape, position, and general characteristics, as being caused by renal stone. The diagnosis of the remainder is dependent on the data of identification given by means of the cystoscope. Furthermore, in the last 100 cases operated on for renal lithiasis, stones were found in 5 cases where they were not shown previously in the radiogram. The types of stone which may not be visible in the radiogram are: (1) The soft secondary stone obscured by complicating pyonephrosis; (2) the small stone, the size of a grain of wheat or smaller, as seen with stone-forming kidneys or so-called oxaluria dolorosa, and (3) cystin and uric-acid stones. Shadows occasionally found, closely simulating that of renal stone, are caused by a calcified area in cicatricial renal tissue, which alone, in all probability, rarely gives rise to much pain. Calcareous deposits in caseated foci with renal tuberculosis may cause shadows which are frequently mistaken for renal stone. Although such shadows may be recognized by their hazy, irregular outline in the radiogram, they can be definitely identified by means of cystoscopic data. Calcareous deposits in hypernephroma were observed in 3 cases as the cause of renal shadows. They are usually to be identified by the various clinical means of diagnosis, particularly the pyelogram. Two cases were observed in which, on exploration, one or more cysts with a calcareous lining were found in the renal cortex, causing a peculiar circular shadow in the radiogram outlining the wall of the cyst. An organized blood-clot with slight calcification giving a hazy shadow, suggestive of a soft stone, was found at operation in five instances.

Among the numerous conditions which may give rise to shadows in the perirenal area, gall-stones are of particular interest. Although it is not our routine procedure to radiograph patients with symptoms typical of gall-stones, it is done whenever the

localization of the abdominal pain is at all suggestive of renal lithiasis. Consequently, we occasionally find shadows in the radiogram caused by gall-stones, and they must be considered in the interpretation of every shadow in the region of the right kidney. The shadow of the gall-stone is often recognized by the following characteristics: (1) High location (on a level with the eleventh rib or above); (2) circular form; (3) multiple overlapping grouping; (4) the periphery of the stone usually casting a more definite shadow than the center, so that the resulting shadow is that of a ring, the center of the stone being invisible. When, however, the gall-stone shadow is single, lies in the area of the kidney, and has the irregular shape and uniform character usually found with renal stone, it may easily be mistaken for renal stone, and pyelography will be found the best and often the only method of identifying its origin. Particularly confusing is the clinical picture when a shadow-casting gall-stone is found coincident with other abdominal lesions or with inflammation in the urinary bladder, as occurred in two cases that recently came under my observation.

*Identification and Localization.*—After demonstrating a shadow, the next step is its identification and, if caused by stone in the kidney, its localization. Although the position of the shadow in question can frequently be ascertained by its relation to the outline of the kidney as seen in the radiogram, because of technical reasons the shadow of the kidney will often be indefinite. If there be a large definite shadow in the region of the kidney, and if purulent urine containing no tubercle bacilli be obtained from the affected side on cystoscopic examination, the diagnosis of renal stone would be reasonably certain. Furthermore, if the shadow were large (an inch or more in diameter), further localization would, as a rule, be unnecessary, since a stone of that size should be readily discovered at operation. However, when a shadow in the radiogram is small, and the urine from the affected kidney is comparatively clear, the shadow requires not only identification, but localization as well. The best method, both of identification and localization of the shadow, is to compare the relation of the shadow in question with that of the injected pelvis, as in pyelography.



The majority of stones in the kidney that are large enough to be visible in the radiogram will cause recognizable changes in the renopelvic outline, as shown in the pyelogram. If no change from the normal is noted, the shadow in question may be considered extrarenal. The abnormality of outline is a consequence of either mechanical obstruction or of inflammatory changes in the tissues. Hydronephrosis, when present, following stone in the renal pelvis, is not, as a rule, extensive, but is usually confined to the distention of the individual calices. Practically every renal stone, whether in the cortex or pelvis, is accompanied by more or less dilatation of the pelvis or individual calices following inflammatory retraction. These changes vary from that of moderate pyelitis to the marked deformity resulting from pyonephrosis. Often the changes in the pelvic outline are the result of both mechanical and inflammatory changes. Not alone will these changes appear in the pelvic outline as the result of stone, but, in consequence of either present or previous infection, more or less inflammatory dilatation of the ureter will also be found. Occasionally the inflammation and dilatation in the ureter may be more pronounced than in the pelvis and of considerable value in determining the intrarenal situation of a doubtful shadow. In only a few instances were inflammatory changes found to accompany renal stone or were so slight as to be of no value in the interpretation. Whereas, in previous years, exploration for renal stone was not infrequently made with negative findings at operation, in the last 58 surgical explorations for kidney-stone made in our clinic stone was found in every instance. This degree of accuracy was made possible largely by means of pyelography.

As a rule, it is comparatively easy, by means of pyelography, to localize stones which are distinctly in the cortex or in the pelvis. It may be difficult to determine whether stones at the end of calices can be removed through the pelvis or cortex. As a rule, with a shadow merging with the end of the calyx, nephrotomy, rather than pyelotomy, will be indicated, and an area of cortical softening is often found adjacent, requiring drainage.

*Coincidence of Renal Lithiasis and Other Abdominal Lesions.—*

When the symptoms of renal stone become acute, the presence of other abdominal lesions may easily be overlooked and be the cause of subsequent confusion. It should not be forgotten that an individual may have two abdominal lesions, as well as one. The presence of both nephrolithiasis and cholelithiasis was proved in 9 patients operated on during the past five years in the Mayo Clinic. The clinical symptoms may be quite definite in suggesting the two separate conditions. Even though the presence of renal lithiasis is evident, if a previous history of pain referred definitely to the right subcostal margin, accompanied by gastric symptoms, be elicited, the gall-bladder should be explored before removing the stone. With cholelithiasis and left renal lithiasis, localization of the pain is usually widely separated, which renders the diagnosis easier.

When a diagnosis of a gall-bladder lesion, as well as a renal stone, is evident, attention should be first directed toward the condition which causes the most acute symptoms. It must be remembered that lesions of the kidney may cause reflex gastric disturbance, though possibly not as often as lesions in the gall-bladder, appendix, and duodenum. Indefinite radiation of pain and reflex gastric disturbance due to lesions of the kidney may be erroneously attributed to a diseased condition in the gall-bladder or appendix. Not infrequently *mild reflex gastric symptoms* exist for several years before acute symptoms of the etiologic renal stone bring the patient to the surgeon. Subacute and chronic appendicitis is frequently found associated with renal lithiasis. When the pain with renal stone is persistently referred to the right lower abdomen, or when the pain has been referred to that quarter for some time prior to its appearance in the region of the kidney, the appendix should first be explored and removed, if necessary. Calcareous deposits in the appendix are frequently found present with renal lithiasis. Symptoms suggestive of intestinal obstruction occasionally appear with severe renal colic. Several patients had been explored for evident obstruction before coming under our observation. In one case a colostomy had been done for evident intestinal obstruction. Even though the existence of

renal or ureteral stone has been definitely demonstrated, if other symptoms suggest another abdominal lesion, an intraperitoneal exploration is justified before removing the stone. It is quite evident that the diagnosis of renal lithiasis is so intimately related to, and so often associated with, disease in the adjacent organs that it becomes largely a matter of abdominal diagnosis, and should be made by one who has had considerable experience in that field.

*Perinephritic infection* resulting from renal stone occurs more frequently than is generally believed. It may be a chronic process, as evidenced by the cicatricial thickening of the tissues and pads of inflammatory fat that frequently are found about the pelvis and kidney. Frequently the perinephritic involvement is acute, and the purulent distention of the perirenal tissue causes severe and continued pain. Long-continued pain with kidney stone lasting over a period of a week or more is often indicative of perinephritic abscess. The patient may bear the occasional renal colic of short duration, but a severe pain persisting over a period of a week or more often brings him to the surgeon. Neither a perinephritic mass nor an enlargement of the kidney is necessarily felt on examination, and but a small pocket of pus may be found at operation as the cause of the severe symptoms.

Bulging of the perirenal tissues or tumor was noted in but a small number of cases. Perinephritic infection is found more frequently with cortical than with pelvic stones. A large branched stone filling the pelvis is occasionally complicated by perinephritic infection, which may be the first clinical evidence of the existence of the stone.

*Value of Urinalysis.*—Visible hematuria was given as a symptom by 141 patients, or 56 per cent. of the total. It occurred with *typical renal colic* in 106 cases, with *indefinite pain* in 24 cases, and *without any pain* in 11 cases. Every case of visible hematuria, therefore, even though pain be indefinite or entirely absent, should be radiographed, regardless of other symptoms. Blood was found microscopically in the urine of 228 patients, or 91 per cent. of the total. In 500 consecutive cases examined routinely who had neither symptoms nor any clinical evidence of kidney lesion

microscopic blood was found in the urine in 146, or 28 per cent. It is found so frequently in the urine as the result of a variety of causes that its presence cannot be regarded as of much practical value. The presence of a few red blood-cells in the urine should not influence us in the interpretation of a doubtful radiographic shadow. Their presence without pain or other symptom suggestive of lithiasis would not necessarily require a radiographic examination. *Pyuria* as a subjective symptom is not of so much practical value, because patients usually confuse the physiologic sediments in the urine with that of pus. The only way to determine the cause of apparent cloudiness in the urine is, of course, by means of microscopic examination. Microscopic pus was found present in the urine of 232 patients, or 93 per cent. of the total; however, as with microscopic blood, the examination of the mixed urine, particularly in the female, will show the presence of microscopic pus in many cases when neither kidney stone nor any other lesion of the kidney exists. Microscopic pus in the urine, although suggestive of lithiasis, is not at all indicative of its presence. On the other hand, the absence of microscopic pus, while unusual with kidney stone, cannot be relied upon to exclude it. It is, perhaps, unnecessary to add that the discovery of small amounts of albumin in the urine is of little or no practical value in the diagnosis of stone.

*Functional Tests.*—It is frequently quite difficult to estimate the functional capacity of a kidney containing a stone and to determine beforehand whether the kidney is to be removed or only lithotomy is indicated. When, on cystoscopic examination, the urine from the affected kidney appears cloudy and diminished in amount, one may infer that but comparatively little renal function remains. It is remarkable how often the urine becomes clear and normal in amount after the stone is removed when cloudy urine was previously seen coming from the affected kidney. On the other hand, the urine from the affected side may appear to be comparatively clear on cystoscopic examination, and at operation widespread destruction of cortical tissue may necessitate nephrectomy. When the pus becomes caseous and oozes out of the meatus only

on massaging the kidney we are usually safe in inferring that nephrectomy is advisable. Not infrequently on meatoscopy no urine will be seen coming from the ureters on the affected side for many minutes—often ten or fifteen. Ineffectual peristalsis of the meatus or continuous contraction may be seen during this period, which is probably best explained by reflex contraction from cystoscopic irritation in a ureter rendered irritable by the stone. One might easily interpret this evident cessation of secretion as due to renal destruction. Stone in the kidney will usually cause marked diminution of functional activity, as demonstrated by the various functional tests. Thus with phenolsulphonephthalein, which permitted a comparatively accurate functional estimate, in many cases of renal stone but one-half of the amount of the dye was returned from the affected kidney as compared with that of the normal kidney. This would lead one to infer that but one-half of the kidney's function remained, and, therefore, nephrectomy might be indicated. In operating on these patients the kidney was often found but slightly diseased, and after operation the normal functional activity returned.

This is an example of the fundamental weakness of all chemical renal functional tests; namely, that functional activity of the kidney can be quite definitely ascertained at the time of examination, but not so its functional capacity when normal conditions are restored. However, the functional test has several elements of value, which should not be overlooked. In cases where there is a total absence or mere trace of phthalein return from the affected kidney, a nephrectomy is usually indicated, even though the urine appears comparatively clear. Again, in cases in which the question arose as to whether or not a shadow was intrarenal, a marked comparative diminution of functional activity on the side in question would be suggestive of renal involvement. Although the majority of stones in the kidney cause more or less comparative diminution in functional activity, occasionally no material difference will be found between the two sides. Equal functional return would not, therefore, exclude the possibility of stone.

## REPORT OF A CASE OF PELVIC KIDNEY: DIAGNOSIS BEFORE OPERATION \*

G. J. THOMAS

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As a means of diagnosing congenital anomalies of the urinary tract the radiogram, following the injection of colloidal silver, is of great value, inasmuch as it demonstrates accurately the position, size, and number of kidneys, and the condition of the ureters. The following case report is an example in which this method was used and the diagnosis made before operation:

CASE A75609.—Female, aged thirty-two, married. Fourteen years previously the patient had been examined in the Mayo Clinic. At that time she had not menstruated. Physical findings: Vagina about one inch in length. No uterus, ovaries, or tubes were discoverable upon palpation. Breasts normal and well developed. Family history: Eight sisters, all having normal menses; five of them were married and had borne children. Present history: Married seven years. No menses, but distress and pain over the region of the ovaries every two months. A year ago, following a cold or wet feet, she began to have attacks of frequent micturition. These attacks lasted six or seven days and then disappeared. She complains of a low abdominal pain, alternating from one side to the other, and she has been confined to bed for two or three days at a time with marked soreness and tenderness in the left pelvis. In sitting down and flexing the left thigh, and in leaning over, she has a severe sticking pain in the left side. She does not sleep well, cannot lie on her left side, is nervous, and tires easily. Examination of urine (twelve-hour specimen): Specific gravity, 1018; 350 c.c., acid, no albumin, no sugar, an occasional red blood-cell. Objective symptoms: Vagina one inch long. No uterus palpable. Rounded mass about the size of an orange high in left inguinal

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fossa, tender to the touch. Slight thyroid enlargement. x-Ray negative. Patient well nourished, but nervous.

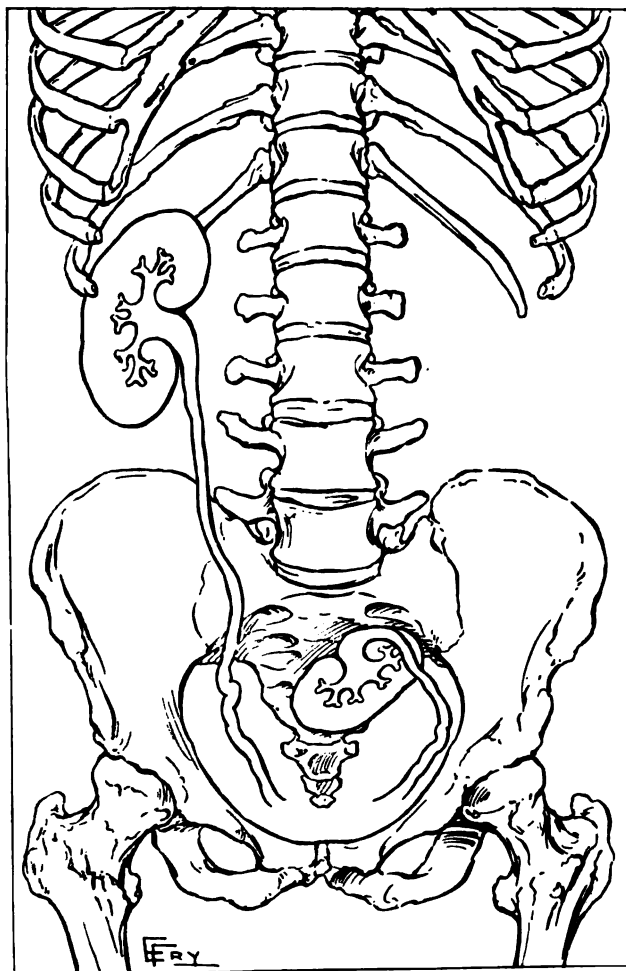


Fig. 119.—Outline drawing of radiogram following injection of colloidal silver into the kidney and ureters. Note position of left kidney in bony pelvis. Normal position of right kidney.

Because of the congenital anomaly of the genital organs without history of menstruation the patient was referred for cystoscopic examination. Cystoscopy showed the urethra and bladder to be

normal. It was difficult to pass the left ureteral catheter more than 5 cm., or  $2\frac{1}{4}$  inches from the bladder. The right side appeared to be normal. Amount and character of the urine from the left side compared favorably with that from the right side. A double injection of colloidal silver by the gravity method was made and a radiogram taken. The passage of the cystoscope and the left ureteral catheter was so painful to the patient that the operation could not be prolonged long enough to give an intravenous injection for the purpose of making a separate estimate of the function of the two kidneys. Fig. 119 shows the pelvis of a hydronephrotic kidney lying well down in the left bony pelvis. The ureter was  $3\frac{1}{2}$  to  $4\frac{1}{2}$  inches in length. The pelvis of the kidney was upward and inward from the cortex, and the ureter's course upward and outward, then downward and inward. The position of the other kidney and the outline of the pelvis, normal.

The patient was operated on November 18, 1912, by W. J. Mayo. The position of the kidney was found as shown in Fig. 119. The pelvis was hydronephrotic and infected; the ureter, about 4 inches long. The blood-supply to this kidney came from two or three renal arteries, from the left common iliac, about one-half inch below the division. The renal vein entered the vena cava just at the bifurcation, and was closely adherent to the kidney-mass. All the left external iliac vein could not be found. It may have become fused with the internal, or it may have been very small, due to the pressure of the adherent kidney.



## ACCIDENTAL INJURIES TO THE DESCENDING PORTION OF THE DUODENUM DURING REMOVAL OF THE RIGHT KIDNEY \*

WILLIAM J. MAYO

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The anatomic relations of the retroperitoneal portion of the duodenum are such that this organ may be injured during operations for the removal of the right kidney. Such injury, however, can occur only if there be infiltration about the pedicle which has caused close adhesion to the duodenum. The duodenum in its descending course overlies the pedicle of the right kidney and a considerable portion of the lower half of that organ on the inner side (Fig. 120). As this portion of the duodenum is retroperitoneal and more or less fixed in position, one can readily understand how the accident might occur under such circumstances. The exact relationship of the duodenum to the right kidney depends upon the mobility of the latter organ, which lies somewhat lower than the left kidney and is more or less movable normally. The extent of this mobility depends on a number of factors. As shown by Harris, the shape of the lower thorax to a large extent determines its position; a loose attachment of the ascending colon to the posterior parietes permits a wider range of motion. Under ordinary circumstances, during a right nephrectomy, the pedicle is loosened until it can be well surrounded with the fingers, clamped with forceps or tied, and as long as this method is followed the duodenum will not be injured. But in those cases in which, on account of infiltration, such a pedicle cannot be formed, it not infrequently happens that the vessels are torn, with a resultant sudden gush of blood, or, after the removal of the kidney, the pedicle retracts from

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the forceps or ligature with sudden hemorrhage, necessitating active hemostasis. As shown by Gerster, if the artery is cut first, the veins may tear, with hemorrhage. In the effort to check this sudden hemorrhage by grasping the vessels with forceps having strong biting jaws and teeth at the end, the duodenum may be seized. As a rule, the injury to the duodenum is not manifested for several days. The injured part becomes necrotic, and a duodenal fistula

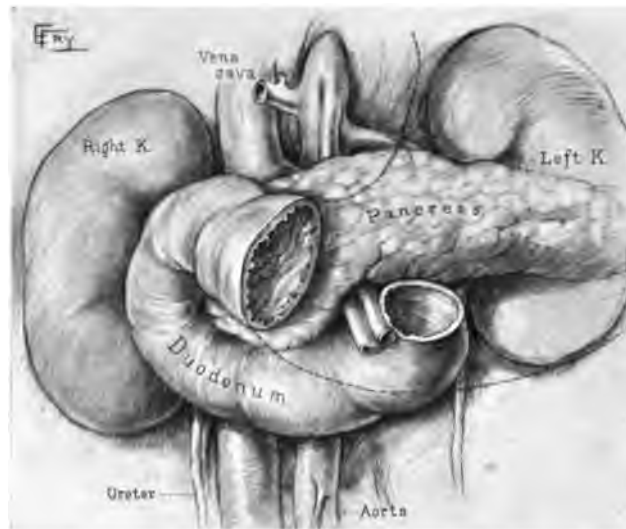


Fig. 120.—Anatomic relation of duodenum to right kidney.

of a most distressing type results, which will often, if not usually, cause the death of the patient.

I have known of three such injuries to the duodenum—the first many years ago, when I was assisting a surgeon who was following a nephrotomy by a nephrectomy. Heavy biting forceps were left on the pedicle. On the fourth or fifth day a copious discharge began of biliary and pancreatic secretions with food discharged as quickly as taken. The patient became rapidly exhausted and died in two weeks.

The second case was one of my own, and the injury occurred

in the removal of a carcinoma of the pelvis of the kidney, the result of a chronic irritation due to a large branched stone. The pedicle was extremely rigid from carcinomatous infiltration, and in the attempt to remove it the vessels were torn across in the infiltrated tissues. With considerable difficulty these vessels were caught by heavy tooth forceps which were left *in situ*. On the fifth day a duodenal fistula showed itself. Biliary and pancreatic secretion and intestinal juices were passed in great quantities. The patient, already in a most serious condition, developed acute nephritis in the remaining kidney and died from asthenia on the tenth day. Necropsy showed a large fistulous opening in the descending portion of the duodenum.

The third case was one of duodenal fistula following nephrectomy seen in consultation. The pedicle had been infiltrated with inflammatory products; the kidney had torn loose. The injury to the duodenum was undoubtedly inflicted by the application of heavy forceps. In this case the fistula was small at first, but gradually increased in size and the patient died two weeks after the operation. One feature in all these cases was the action on the skin of the escaping secretions. Large areas of the neighboring integument became scalded, painful, and irritated. In one patient this set up a rapidly spreading eczema, and in a week a great part of the skin of the body was affected.

From the fatal issue in these three cases it would seem that accidental injury to the duodenum in connection with right nephrectomy is an exceedingly serious occurrence, and although after a somewhat careful examination of the literature I have not found cases reported, I can but believe that this accident is more common than the records show and that some of the cases in which fistulas have formed following right nephrectomy, while supposedly in other portions of the intestinal tract, have really been duodenal. It will be noted that in the three cases herein mentioned duodenal injury took place during attempts to check hemorrhage, and probably all of them were due to forceps.

In this connection I would say that in the same manner the vena cava is even more frequently injured. When the pedicle is

infiltrated, the renal veins may tear away from the vena cava and the latter be grasped in forceps in attempting to stop the bleeding. On the left side the vena cava is not thus exposed to injury, since the veins are sufficiently long to cross the abdominal aorta to the left side of the body. Infiltration, either from infection or carcinoma, which causes a shortening of the pedicle containing the blood-vessels, makes the formation of an adequate stump difficult and is the most common cause of the sudden hemorrhage which leads to the inaccurate use of the forceps and injury to the duodenum. Since the occurrence of the injury in the second case mentioned, I have tried to avoid the use of forceps in the first effort to control the bleeding from slipping of the ligature on the pedicle. As a matter of fact, forceps is seldom necessary for the immediate control of hemorrhage of this character. The fingers are so accurate and so sure a means of temporary hemostasis that they should be depended on and the forceps used only to clamp the vessels after they are caught by the fingers.

In vessels the size of the renals one has little difficulty in following the stream of blood directly to the pedicle, and in its pulsation the artery fairly jumps into one's fingers. In these cases the veins are usually tied to the artery by the infiltration, and the whole pedicle can be thus secured with surprising ease. During the period in which inadequate incisions were used for nephrectomy I had the misfortune a number of times to lose control of the pedicle of the kidney during the enucleation, with sudden hemorrhage following, and never failed to grasp the vessels promptly with my fingers. This is quite true of other vessels of the same size. The larger the vessel, the more easily it can be grasped, as during systole the vessel is pushed forward as though for the purpose.

In the removal of large pelvic tumors and rectosigmoidal carcinomas, I have, on several occasions, had a torn or divided internal iliac to deal with, and was always able, even with the hand deep under the tumor, to grasp and hold the vessels until the tumor could be removed and the arteries and veins accurately secured. With an adequate incision for the removal of the kidney, such as I have previously described, injuries to the duodenum or failure

accurately to secure the vessels will seldom occur. Division of the structures behind the twelfth rib, combined with transverse incision (Fig. 121), mobilizes the lower wall of the chest, and with the patient lying on the loin of the opposite side, well elevated in a saddle, nephrectomy has been made a safe procedure because it is done under the eye.

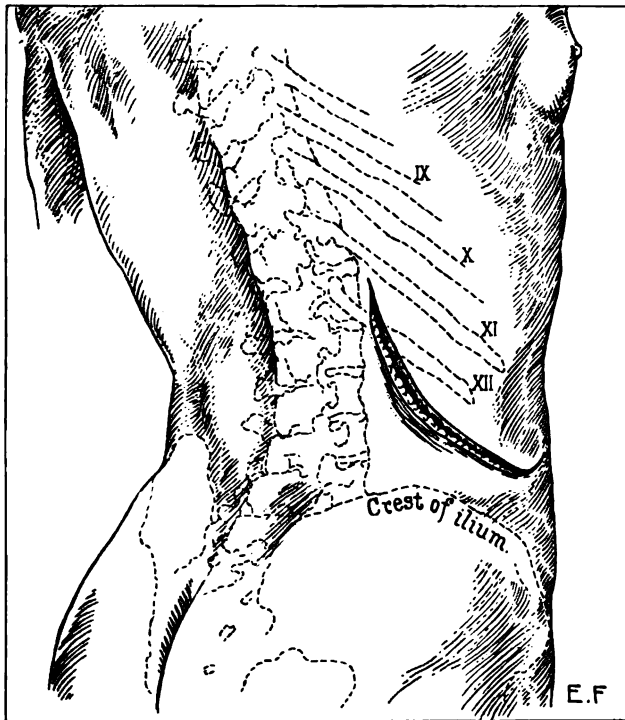


Fig. 121.—Incision for operation on the kidney.

In two classes of cases, however, injuries to the duodenum as well as the vena cava are liable to occur. When fixation and shortening of the pedicle take place as the result of inflammation, usually in cases of pyonephrosis with stone, and especially following nephrotomy for such a condition, the attempt to remove the kidney in the ordinary manner renders accidents in securing the

pedicle not infrequent. Nephrectomy secondary to nephrotomy, especially when complicated by fistulas, is exceedingly difficult. In Tuffier's Clinic, nearly fifteen years ago, I first observed such cases handled properly, that is, by means of a *subcapsular* nephrectomy. If the disease for which the kidney is to be removed is neither malignant nor due to tuberculosis or other disease, which requires removal of the capsule, it is comparatively easy and safe to continue the outer incision into the fatty and fibrous capsule of the kidney, and then to enucleate the entire kidney from its bed in the firm surrounding wall, securing the pedicle in the hilum of the kidney itself. Under such circumstances it may occasionally happen that the kidney is completely separated before the pedicle is secured, and there may be little hemorrhage from the vessels at the point where they have pulled off. If severe hemorrhage does occur, the firm rigid cavity lends itself to the control of the bleeding upon pressure either by the fingers or by a piece of gauze held in the fingers. By sliding the fingers from below up, the mouths of the vessels can readily be seen and controlled with forceps or suture. Were one working outside this firm capsule, no such control could be exercised over the vessels, which would promptly retract, adding to the difficulty of securing them. When there is much infiltration and subcapsular nephrectomy is not advisable, the peritoneal cavity and sometimes the pleura may be opened. It is always necessary, therefore, after separating the kidney, but before its removal with possible soiling of the field, to examine carefully to see that there is no opening into the peritoneum. The pleural cavity, which, fortunately, is very rarely injured, makes itself manifest by a sibilant sound when the air rushes in and out during respiration, so that this injury is not liable to be overlooked.

The kidney is held in position, first, by its fatty capsule; second, by the ureter; and third, by the blood-vessels. In doing nephrectomy the separation should be made in the following sequence: the kidney, loosened from its bed until it is held only by the vessels and the ureter, the ureter then pulled to the surface, caught between two clamps, sterilized with phenol (carbolic acid),

and both sides tied. The clamp is not to be left on the side of the kidney, since it may be pulled off during the further course of the operation with soiling of the field. By thorough separation of the perirenal adhesions the vascular pedicle can, as a rule, be easily secured in a small mass.

In the removal of carcinoma of the pelvis of the kidney injuries to the duodenum and vena cava are most liable to occur. The most frequent malignant tumor of the secreting structure of the kidney of the adult is the so-called hypernephroma, more properly termed renal mesothelioma, as pointed out by Wilson. We should remember that the kidney is formed from two entirely separate anlagen. For a long time it was thought that the entire kidney was formed from a diverticulum from the Wolffian duct. It is now known that only the ureter, pelvis, calices, and straight tubules are so formed, *i. e.*, only that part of the kidney which collects the urine has its origin in the Wolffian duct. The secreting structure of the kidney has a far different origin—in the nephrogenic tissue, which is mesothelial in origin. Therefore, we have two entirely different types of malignant disease of the kidney, one having its origin in epithelial structures, a true carcinoma, and the other arising in mesothelial tissue, which has been incorrectly termed hypernephroma, a malignant disease of the secreting structure of the kidney which has some general similarity in morphology to tumors of the adrenal body. Grawitz, in 1883, first called attention to the resemblance between these growths and the adrenal body, and under his influence these tumors were called hypernephromas. Stoork and Wilson have shown, however, that the adrenal body is formed in what is later to become the pleural cavity, and that it is always separated from the kidney by a complete histologic membrane, and, further, that these so-called hypernephromas always occur in the renal substance and not in the fibrous capsule of the kidney, where such supposed adrenal remnants are most frequently found. Also, that such tumors are rarely found in the adrenal body itself, and when so found, give an entirely different picture clinically and pathologically from the ordinary tumors in the kidney which have been called hyper-

nephroma. That true hypernephromas or tumors of the adrenal body and of adrenal rests in the kidney may be found there is no question, but they are extremely rare. It now seems proved beyond reasonable question that the so-called hypernephroma of the kidney is, in most instances, mesothelial in its origin, and, unlike carcinoma, seldom involves the glands until very late, but tends to spread by means of the blood-stream, as would be expected in tissue so closely related to the connective-tissue group. Nephrectomy for large tumors of this description is usually best accomplished by some type of transperitoneal incision, because the tumor presents anteriorly, crowding into the abdominal cavity. The incision outlined in Fig. 121 can be brought well forward toward the median line, and, if necessary, supplemented by a straight incision in the right rectus muscle, or a long transperitoneal incision at the outer border of the rectus muscle will be found satisfactory. The ascending colon is separated and drawn to the inner side. The ureter is double tied in its course and cut between. The lower portion of the growth is separated on its inner side and the upper fragment of the ureter followed to the renal artery and vein. These vessels are dissected out, tied, and divided before the growth is removed from its bed.

During the removal of renal mesotheliomas accidental injury to the duodenum will not often take place, because the pelvis is seldom involved in the disease. But when we come to the group of carcinomas, true epithelial proliferation which involves the pelvis, the calices, and other structures having origin in the Wolffian duct, an entirely different picture is produced. In 85 per cent. of our cases apparently this type of cancer was the result of a chronic irritation from stones in the renal pelvis. Here infection and ulceration of the pelvis and secondary involvement of the connective tissue in the pedicle lead to fixation and shortening of the pedicle, together with adhesion to the neighboring viscera on the right side, and sometimes to the duodenum in its retroperitoneal portion. In such cases subcapsular nephrectomy is inadequate if we are to give the patient a chance for cure. The kidney and capsule, with the pelvis and an adequate portion of the ureter,



must be removed, and it is in these cases that the duodenum will be endangered, even in the hands of the most expert and careful surgeon.

When this accident occurs, what can be done to repair the damage? Here is the crux of the problem. As a rule, the duodenal injury is not made manifest until several days after the operation. The character of the fistula does not lend itself to spontaneous healing, the gastric, intestinal, pancreatic, and biliary secretions in combination rapidly enlarge the opening, irritate the skin, and exhaust the patient. As shown in the postmortem on the second case mentioned, the fistula was large, infiltrated, and, of course, without peritoneum. In a similar case I should, before the patient becomes exhausted, make a transperitoneal attack on the fistula itself, lift the descending duodenum from its bed, suture the opening, and transplant a flap of peritoneum or omentum across the suture-line and finally make a jejunostomy for temporary feeding purposes.

It does not take much imagination to suggest and draw on paper various methods of multiple short-circuiting operations, but at the operating table, with the patient in the condition which would probably exist under such circumstances, the carrying out of such schemes would be sufficiently uncertain to make us careful to avoid the accident.

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## NON-PAPILLARY BENIGN TUMORS OF THE BLADDER \*

E. S. JUDD

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Tumors of the bladder are classified into three main groups: (1) Epithelial tumors; (2) connective-tissue tumors; and (3) muscular tissue tumors.

The first group (epithelial) comprises the carcinomas, papillomas, adenomas, and cysts. The first two of this group are by far the most common tumors of the bladder, making up about 90 per cent. of the total.

The second group (connective tissue) contains the sarcomas, myxomas, fibromas, and angiomas. The sarcomas are occasionally seen in children, though these tumors are rare.

The third group (muscular tissue) contains those tumors which spring from the musculature of the wall of the bladder and make up between 1 and 2 per cent. of all specimens.

Of these vesical neoplasms, including all these groups, we have seen 164 cases. Two of these were of the non-papillary benign type, which spring from the muscular layer of the bladder. It is the tumors of this group I wish to report at this time.

### REVIEW OF LITERATURE

In a fairly extensive review of the literature we have found about 30 cases reported.

Watson reviews 653 collected cases of tumors of the bladder. Twenty of these were myomas. In 16 of these cases the tumors were removed by suprapubic operations, not resections; 13 of these patients survived; 5 are reported as having recurrences.

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Three were free from recurrences less than one year. Three were free from recurrences more than one year. Four were operated on by suprapubic bladder resections; 3 survived. There were 2 reported recurrences: 1 survived six years. This report would seem to indicate that these tumors are malignant, or at least recur locally, and in that respect simulate the common tumors of the bladder of the epithelial type. In most of the other reported cases the patients have remained well indefinitely. Both of our patients are well now over two years without any signs of recurrence, and we did not believe from the microscopic and histologic examinations that these tumors should be called malignant.

A single similar case is reported by Gotzl. He states that of 26 reported cases, he found only 2 had had a probable diagnosis before operation. His patient had four small tumors situated near the urethral orifice. These were covered by intact mucous membrane.

Mandelbaum makes the statements that myomas are not common, that they may be single or multiple, that they are covered by normal mucous membrane, that they arise directly from the muscle-fibers of the unstriated variety, but that rhabdomyomas have been seen.

Davis mentions one case in a series of 41 tumors of the bladder.

Keyes, referring to the pathology of tumors of the bladder, says that myoma is usually benign, and that the tumor may be intravesical, interstitial, or subserous, and, like vesical fibroma, may pass unnoticed unless it interferes with the mechanism of urination.

Blum reports a case of a young man whose symptoms were severe bleeding and considerably increased temperature. An edematous tumor the size of the fist and with a twisted pedicle was found in the posterior wall of the bladder. He says the submucous type is the more common.

Bohme reports one case operated on, and that the patient remained well after operation.

In most of the reported cases, as in our two, bleeding was the first and most marked sign in spite of the fact that no distinct

ulceration of the mucosa of the bladder was found. The bleeding, we presumed, came from the congested mucous membrane of the entire bladder, especially about the tumor.

Starting in the muscular layer, these tumors may extend into the bladder and outward into the peritoneal cavity. They may attain considerable size, as in one of our cases the tumor could be palpated above the pubic bone and was as large as an ordinarily distended bladder. Because of the rarity of these cases we have had much difficulty in finding detailed descriptions in the literature; the deductions, therefore, have been largely drawn from our two cases.

The location of the point of origin in the wall of the bladder in these cases was close to the meatus of the urethra—just above the left lobe of an enlarged prostate in one case, and, in the other case, about one inch above the urethra. In both instances the tumors were suspended on distinct pedicles. The larger tumor, which almost completely filled the bladder, was attached to the bladder-wall by only a pedicle about two-thirds of an inch in diameter. The tumors were single, and the mucous membrane of the exposed surfaces was apparently normal.

*Symptoms.*—Our histories show that the characteristic symptoms of tumor of the bladder were present. Definite hemorrhage was present in both cases. There were more difficulty and frequency and irritability than usual in most cases of other types. One patient had had trouble for four years and the other for five years. The bleeding was painless, except for clots, though it was very severe in both cases. The blood was bright red. Between the attacks of bleeding, which usually lasted a few days, the urine cleared up completely and several of the specimens examined microscopically showed no blood. One patient had experienced repeated very severe hemorrhages for over three years and was quite anemic. Pain became severe, and evidently was caused by obstruction to the urethra. Catheters had been used in both instances, though only occasionally until just before coming for treatment.

Frequency from thirty minutes to one and one-half hours had been gradually getting worse in one case, and the other patient

was obliged to use a catheter continuously for several days before our last examination. This may have been due to the enlargement in the prostate, which was evidently a part of the trouble.

In summing up the clinical symptoms we find that these patients had the same symptoms which accompany other tumors of the bladder except in one point, and that was the bleeding. The bleeding in both of these patients came as a very sharp and severe hemorrhage. Each had bled down to the point of extreme weakness several times. I do not think we have seen in other cases of lesions of the bladder or kidney so much bright red blood passed in such a short time.

*Diagnosis.*—The diagnosis, though at least suggestive, could not be established to a certainty in either of these cases until an exploratory incision was made. In the first case of smaller tumor which was associated with an enlargement in the prostate there was so much bleeding as soon as the cystoscope was introduced that the field was entirely obscured, and we were obliged to operate on this patient almost as an emergency to stop the bleeding.

In the second case, a male fifty years of age, the neoplasm was so large that it almost completely filled the bladder. Its surface was smooth and appeared just the same as mucous membrane lining the walls of the bladder, which was congested and inflamed. The capacity of the bladder was from 6 to 8 ounces, and there was no apparent abrasion in the mucous membrane at any point. A parallel case had not been seen before, but it was thought more than likely that the tumor, which was easily palpable above the pubic bone, was extravescical, and pressing well down into the bladder. There was also much bleeding during this examination, and clots seemed to be squeezed out of the roof of the bladder. The bulging was more on the right side. Clear urine was coming from both ureters.

*Treatment.*—The first patient was examined in our clinic, August 2, 1907. We endeavored to check the hemorrhage and get him into better condition before operating, but repeated washings of the bladder with different solutions seemed only to make the condition worse, while the patient was getting continually weaker

and suffering greatly from clots. His hemoglobin was under 50 per cent. Under primary ether anesthesia we made a large suprapubic incision. The peritoneum was stripped back from the bladder and the bladder opened as usual. After cleaning out the blood-clots the tumor, which was about an inch in diameter, was seen attached to the right anterior wall of the bladder. This was held higher into the bladder by an intravesical enlargement from the prostate. It was first thought that the enlargement of the prostate and the tumor could be enucleated together. In starting the enucleation the tumor was freed from the bladder as soon as the mucous membrane had been separated. It was then seen that the tumor was on a pedicle suspended from the wall of the bladder, and that it was not connected with the prostate at any point. The enlargement in the prostate was then removed. The bleeding stopped within a short time, and it was not necessary to pack. A double catheter was introduced into the urethra; the suprapubic incision into the bladder closed loosely with catgut, and a rubber tissue drain placed down to the incision. After the operation there was very little bleeding; the urine was clear in a few days. The rubber tissue drain was removed on the third day. There was slight leakage from the wound only during the first week. The patient left the hospital on the sixteenth day, the wound being practically healed. He was discharged from our care at the end of three weeks. This man has been perfectly well since the operation. The last communication from him was dated November 24, 1913.

The second case was examined January, 1912. Because of the uncertainty of the location of the tumor, a suprapubic incision was made for an exploration. On opening the peritoneum it was readily seen that the large, rounded tumor was within the bladder itself. The kidneys were palpated to rule out a possibility of hemorrhage from a renal tumor. They were found to be negative. The peritoneum was then closed and packed off, and the bladder was lifted up into the abdominal wound. A large incision in the roof of the bladder was necessary for the removal of the tumor. The surface of the tumor was smooth, and its appearance the same

as the wall of the bladder. The pedicle was caught in a pair of clamps and the tumor removed. There was very little tendency to hemorrhage, and a few catgut stitches in the wall of the bladder at the point of attachment of the pedicle controlled all oozing. As the bladder was dry, the wound in the dome was closed completely, a rubber tissue drain being left in the space of Retzius down to the opening in the bladder. Urine drained from the wound for some little time, and it was several weeks before it completely closed. After this rather slow convalescence the patient made a complete recovery. He had a little frequency and burning after going home. This man recently reports that, as far as he knows, he is entirely well.

*Pathology.*—The two tumors were very similar in structure. The smaller one (Fig. 122) weighed 40 grams; the larger (Fig. 123), 230 grams. They were rounded and very firm and hard, and covered by stratified mucous membrane similar to the mucosa of the bladder. On cutting into the tumors they were found to have the same density throughout, and with very much the appearance of uterine myomas. Histologically they were composed of smooth muscle-fibers and fibrous connective tissue (Figs. 124 and 125). The smaller tumor was much the more fibrous (Figs. 122, 123, 124, 125).

#### CASE REPORTS

CASE I.—A446. Male, aged sixty-one years. Date of first examination, August 2, 1907. Occupation, manager of an opera house. Previous disease, pneumonia two years ago.

*Subjective Symptoms.*—Some bladder trouble for five years starting with frequency and instability at times. Complaints of difficulty in controlling bowels when passing urine. Pain before urination. Lost ten pounds in past year. At times passes much fresh blood. At this time an examination of his urine showed pus and blood. *Hemoglobin*, 50 per cent. After this examination we did not see him again for four years. November 28, 1911, we again examined him, at which time he said his symptoms had improved greatly after leaving here. Bleeding had ceased, and he had only occasional difficulty in urinating. During the past month, however, he had been much worse; chills and



Fig. 122.—(Case A446.) Gross section through tumor of bladder.

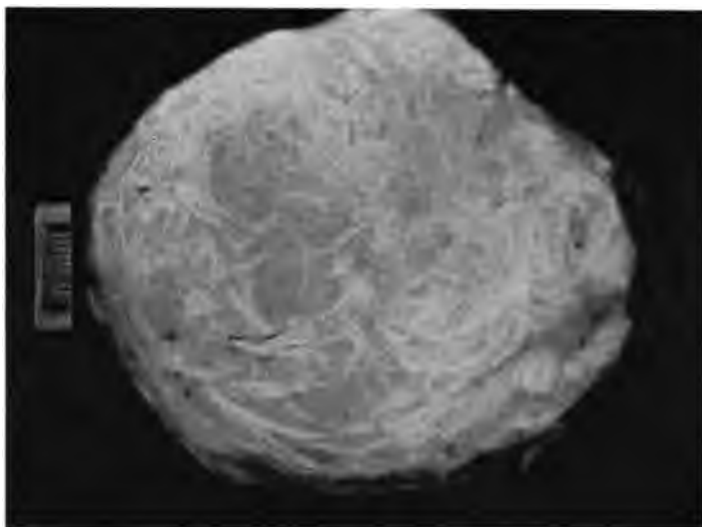


Fig. 123.—(Case A62897.) Gross section through tumor of bladder.



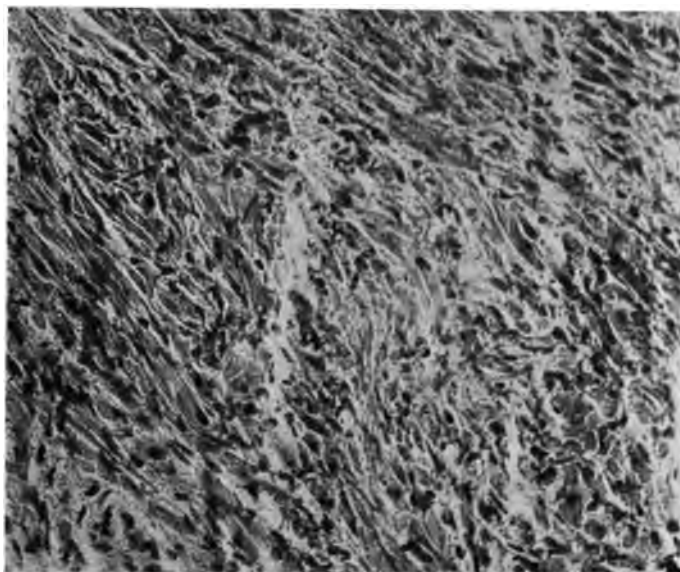


Fig. 124.—(Case A446.) Microscopic section ( $\times 250$  diam.) of tumor of bladder.

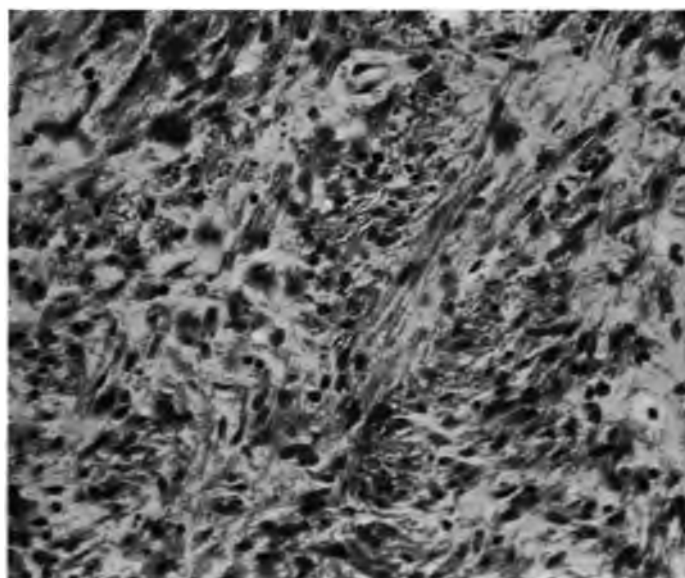


Fig. 125.—(Case 62906.) Microscopic section ( $\times 250$  diam.) of tumor of bladder.

fever, and much blood in the urine. Had used a catheter entirely for the past five days, and was able to pass only a few drops without it. A week before returning he had had nausea and vomiting. He feels weak, and has lost 15 pounds in the last month. Examination of specimen at this time gives specific gravity 1020; reaction acid; albumin+; erythrocytes++.

*Objective Symptoms.*—Bilateral enlargement of prostate, smooth and soft. *Cystoscopic:* Prostatic enlargement, bilateral 3, intravesical 2, on a scale of 4. Bleeding raw surface of the left side of the bladder. *Blood-pressure* 150. *Diagnosis:* Prostatic enlargement.

**CASE II.**—No. A62897. Male, aged fifty years. Date of examination, January 9, 1912. German farmer. Family history negative. Previous diseases none.

*Subjective Symptoms.*—Comes for urinary difficulties with past history of repeated hemorrhages. Four years ago some moderate pain low in the right fossa. Three years ago painless hemorrhage of bright red blood from the bladder, then no signs of any kind for two years. In the fall of 1910 second hemorrhage, consisting of dark clotted blood, lasting five weeks. No pain. In the spring of 1911 hemorrhage lasting several days, and then off and on for several months. In the past four months much trouble and pain on account of obstruction, both in passing of urine and obstruction to catheter. Painful experience four months ago on account of hemorrhage and obstruction, clots and spasms. Occasional fever. Temperature, 102° F. at times. Much difficulty in urinating. Three weeks ago showed a growth in the bladder. Increasing frequency. Loss of weight, 10 pounds.

*Objective Symptoms.*—Pallor, large movable mass in suprapubic region a trifle toward the right side. *Cystoscopic:* Mucosa shows chronic inflammation. No evidence of cancer or papilloma. A very large smooth bulging mass, as though the entire roof of the bladder were being pushed down. Much bleeding in clots seems to come from roof of the bladder. *Diagnosis:* Tumor in suprapubic region, either a part of the wall of the bladder or else extravascular pushing in the dome of the bladder. *Urine analysis:* Specific gravity, 1012; acid; considerable albumin.

In concluding, it seems that these two cases are of sufficient present interest to report because of their rarity. Of our entire series of 164 vesical tumors, they form 1.2 per cent. While they

are rarely seen, it should be borne in mind that this condition is suggested in sharp, severe, painless bleeding from the bladder, not associated with other symptoms. It seems to us that it will always be difficult to make a positive diagnosis of the exact lesion in these cases without first exploring the bladder.

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## EXCLUSION OF THE BLADDER, AN OPERATION OF NECESSITY AND EXPEDIENCY\*

CHARLES H. MAYO

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Exclusion of the bladder is an operation which has been slowly accepted by the medical profession, and while it is generally admitted that such an operation may be necessary and often is advisable, the mortality following the earlier procedures was at least detrimental to enthusiasm. However, there has been much more to overcome than mortality in the matter of sentiment and the so-called conservatism which urged the preservation of the bladder at any cost regardless of control or comfort.

The natural mortality in these cases, although high in deformities and assured in malignancy, was, at least, not the work of man. Oppel, quoting Mirotworzeff, gives the statistics as follows: "Seventy patients between 10 and 20 years, 10 deaths; between 20 and 40 years, 17 deaths; between 40 and 50 years, 5 deaths; one reached the age of 70 years." He states further that the natural mortality in cases of exstrophy of the bladder in children show that more than half die before the tenth year.

Within a comparatively recent period our interest in the subject has been revived by reports of many successful cases of exclusion of the bladder and with the improved technic of the various procedures. To determine the best method of disposal of the secretion of the kidneys in individuals in whom it is necessary or expedient to exclude the bladder, is still one of the serious problems of surgery. To say, however, that the modern operation exposes the patient to greater danger from in-

\* Read before the American Surgical Association, May 8, 1913. Reprinted from *Annals of Surgery*, July, 1913, pp. 133-144.

fection than is compensatory with the mitigation of his suffering, together with the natural mortality of the disease, is not consistent with the history of the patients or the records of the progress of surgery in these cases. Unfortunately, many of the patients under discussion are already suffering from the secondary infective complications before operative measures are advised. The patients under discussion may be grouped under three headings (Fig. 126):

(1) Those suffering from congenital anomalies of the bladder or urethra of such character as not to permit restoration with controllable urine or who cannot be relieved from painful sequelæ by local surgical or other measures.

(2) Those in whom portions of the ureter are necessarily or accidentally injured or removed during abdominal, pelvic, or sacral operations.

(3) Those in whom malignant disease of the urinary bladder is too extensive to permit removal by partial resection of the bladder with retentive function under control, and those in whom gross malignant or other disease of the bladder exists, but in whom the power of retention and control adds to their suffering. These cases will necessarily be limited in number.

For the repair of the first group various surgeons have devised a wonderful variety of ingenious methods. Making a bladder from skin-flaps was originated by Roux in 1852. Various modifications have been developed by Thiersch, Nélaton, Wood, and many others. The compression of the bony pelvis (the anterior portion of which is usually missing) was instituted by Passavant, the breaking and subcutaneous section of lateral bony arches were devised by Koch, König, and others, and Trendelenburg successfully accomplished the closure of the bladder, covering it with an anterior bony arch by freeing the sacro-iliac joints. Epispadias, especially in the female, which is so extensive as to cause a loss of urinary control, is also placed in this group, although a few of these cases may be benefited by local measures.

Excellent results have been claimed for the Goebel method of providing a voluntary sphincter made from the pyramidal

muscles. Soubbotin's method, in its effort to develop a bladder with control of the sphincter, is probably the most ingenious. It is especially applicable in males. An anterior incision is made



Fig. 126.—Exstrophy of bladder in male. Exposed mucosa with ureteral openings.

within the anus, the space in front of the rectum and within the sphincters is tunneled up to reach the base of the bladder, a rectangular strip, of which the future urethra is made, is drawn down

to protrude from the anal ring in the fore part of the rectal opening. The remainder of the bladder and the anterior part of the rectum are converted into a closed pouch, the control of which is contained in the rectal sphincter. The operative mortality in these cases is 25 per cent., and should the technic fail, the patient is exposed to the loss of control of both bladder and bowel, since no other operation is then possible. The new bladder is exposed to infection by all the intestinal flora through its short urethra. The plan of Gersuny involved the same principle of utilizing the anal sphincter to control the open end of a separated loop of bowel to which the ureters were attached.

The objection to any method of operating for the repair of these defects which does not control urine automatically is a very serious one. Uncontrollability of the urine is only accepted by the patient who acquires the condition as the lesser of two evils—a greater one being the pain due to its retention or delivery. If an uncontrolled bladder be made from an exstrophy, the patient is no better off, and, if anything, worse than a high epispadias, since the more perfectly an uncontrolled bladder is developed the more surely will it become infected or filled with stone or phosphatic concretions from the decomposing urine. He thus becomes more liable than before to an ascending infection and develops conditions which require the reopening of the bladder.

The cloacal condition, which exists normally in fowls and is also the condition which exists during the first weeks of the human embryo, early suggested the thought of making such a deflection of urine through the rectum. Such a method secured a retentive space under control, and was comparatively easy of accomplishment.

The high mortality from ascending infection of the kidneys through the ureters following the old methods of intestinal union made the procedure almost prohibitive, especially when complications were increased by shock and peritonitis. Some of these patients were already debilitated by the infection of one and sometimes both kidneys or their pelves. Woolsey reported stones in both ureters in a case of exstrophy of the bladder, and a

patient with epispadias, having stones in the kidney, was observed in our clinic.

In order to obviate these risks in cases of exstrophy, Maydl (1892) removed the base of the bladder with the ureters attached and transplanted the segment into the rectum as a transperitoneal operation, the ureteral openings being considered as the valves. Other surgeons have projected the area of bladder into the rectum extraperitoneally, the wall of which was closed around the ureters or it was transposed and sutured into the incised rectal wall of which it became a part. Since the majority of the patients in this group are males, they lend themselves readily to such treatment. Russian surgeons, using Maydl's method, report 32 per cent. mortality. Orlow reports 17 per cent. mortality in 61 cases, and Drucbert's analysis of 81 cases gave 27 per cent. of deaths within fifteen days of the operation.

More recently Moynihan has converted much larger areas of the bladder into the wall of the rectum, thus increasing its capacity (Fig. 127). This operation was varied by Lendon, Peters, Sherman, and others by removing the ureters from the wall of the bladder, including a small area of attached mucosa which is projected into the bowel. These operations were usually performed extraperitoneally, though Jaja converted the method into an intraperitoneal one. In reporting several cases done by the Lendon-Peters method, Buchanan credits Bergenhem of Nykoeings with having antedated them by five years (1894). The posterior operation has been performed by Knaggs through the Kraske sacral resection. Various methods of uniting the base of the bladder or ureter with the anterior rectal wall have been devised, for example, the Boari spring button to develop a permanent vesicorectal fistula within a small closed bladder or a ureteral-rectal one by suture, or by the necrosing due to the pressure of forceps. Some surgeons have aimed at half a loaf by extirpating the bladder after having united the ureters with the vagina, as did Pawlik, Sommers, Chavasse, and others, or with the inner end of the urethra, as done by Sonnenburg. Interesting and ingenious methods have been advocated by Rutkowski and other



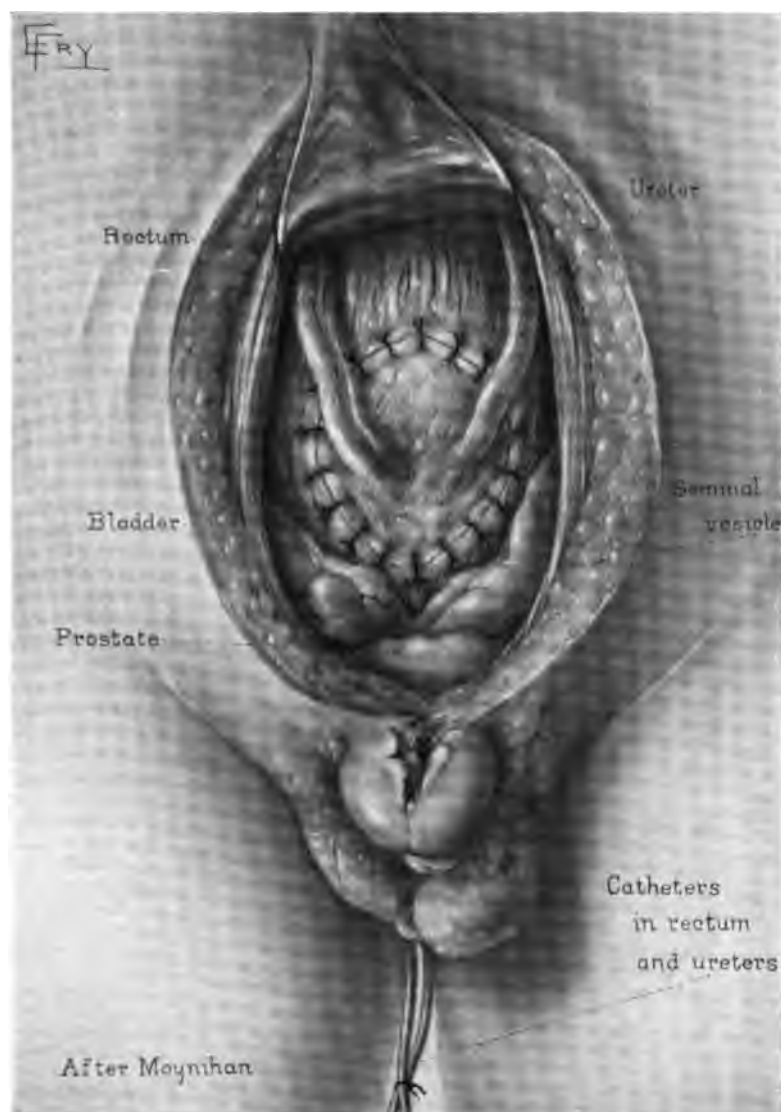


Fig. 127.—Segment of bladder with ureters inserted into anterior rectal wall.

observers, for example, developing bladders from portions of intestine which are separated from the fecal flow by double section and closure with anastomosis of proximal and distal ends of intestine. The new bladder is supplied by its attached mesentery, and the ureters are anastomosed with it. Connell showed experimentally that unilateral attachment of the ureter was simple, but fatal if the second ureter was also united.

In case the cecum is thus employed, as in a case reported by Makkas (1910), an appendicostomy is made through which the urine is drawn by a catheter passed at regular intervals of a few hours. Surgeons have endeavored to develop a form of cloaca by section of the sigmoid several inches above the rectum, closing the distal end and anastomosing the proximal end to the bowel just above the rectum. The ureters are then attached to the blind extremity, thus aiming to avoid direct fecal contamination. While the urinary flow may wash out the regurgitant feces, the natural tendency of attached sections of the bowel, out of circuit, is to impact, and in that event the desired result would not be obtained.

In the second group of cases are those in which something must be done with the injured ureter when it cannot be reunited to itself or reattached to the bladder, as will occur in the occasional case. The injured ureter may be reunited with the other ureter if that is patent, or one or both ureters may be united to the colon. Mirotworzeff and Tichow believe that it is best to unite the ureters to the pelvic colon and that evacuations should be fairly frequent to avoid absorption. Berg demonstrated that when the urine traversed the entire length of the large bowel, urinary intoxication occurred, which would indicate that the methods used to unite an injured ureter to the end of the appendix are more ingenious than practical, offering no advantages over older methods which have failed. This is also true of the technic used in Fink's fatal case, in which the base of the bladder-exstrophy was united to the appendix.

Under some circumstances, the remaining kidney being healthy, one ureter may be tied, causing the death of the kidney. Many

observers believe that by whatsoever method the ureters are attached to the bowel they will frequently transmit infection to the kidney or its pelvis. In this connection Oppel's report is interesting, showing that some pyelitis is common following ureteral anastomosis and that autopsies made years afterward show that the conditions may clear up without a trace of their effects on the kidney.

Direct drainage of the urine to the skin was advised by Balance and Edwards in 1886. This has also been accomplished by pelviotomy and by Watson's nephrostomy. In 1896 Harrison performed the operation and deflected the ureter to the skin of the loin after tying the other ureter. The method was later repeated on both ureters by Bottomley and also by Rovsing without their knowing of Harrison's work. These operations were done both transperitoneally and extraperitoneally, the urine being collected by special apparatus. The operation is a simple one, and can be done in two stages, that is, one kidney or one ureter at a time; the bladder being dealt with or not, according to the condition present. Bovee has collected 13 cases of cutaneous ureterostomy.

The patients in the third group, namely, those having malignant disease of the urinary bladder, form an interesting and complicated series. Transplanting one ureter into the bladder is no longer a rare operation. Such procedures are satisfactory for the suitable case, in which a controllable bladder will be retained, but other methods are necessary for those patients in whom all of the bladder must be removed or in whom life can be prolonged and comfort secured even though the condition be too far advanced locally or by metastasis to warrant radical procedures.

Tichow and Grammatikati report 61 cases of neglected cancer of the uterus in which the vagina, bladder, uterus, and lymphatic glands were removed and the ureters implanted into the rectum. The mortality was 30 per cent.

The history of the various attempts to transplant the ureters to the bowel is a long one. From a perusal of the voluminous literature on the subject it would appear that the best theoretic

and practical operations, when they can be employed, are those which permit the ureters to traverse some distance between the mucosa and outer wall of the bowel before penetrating its lumen or are infolded by the wall of the bowel for a space, and next those



Fig. 128.—Double implantation of ureters (after Martin).

methods in which the base of the bladder is transposed and made a part of the rectal wall.

Ureterostomy and nephrostomy to the back is a procedure which may be recommended for special conditions, such as a diseased colon, advanced cancer of the bladder, or of double tuberculosis of the kidney and bladder.

In the year 1790 Petit called attention to the valve-like open-

ings of the ureters, and it is nearly a half a century since uretero-rectal and vesicorectal anastomoses were made by Simon, followed later by Lloyd and Johnson. The variety of the valve type of operation was also reported by Fowler (1898), Martin, Carl Beck (1899), and later by Frank. Coffey has made an extensive investigation concerning the valve function of the duct-openings of both the common duct of the liver and of the pancreas. He has proved experimentally and mechanically that the valve effect is caused by the extension of the duct for some distance between the mucosa and the muscularis (Fig. 128).

Cabot has shown that the ureter is similarly placed in the wall of the bladder for a distance of 1 to 1.5 cm. Direct transplantation of the ureters failed in not providing for compression of the ducts by internal pressure, thus permitting dilatation of the ureters and regurgitation into them. The method of transplanting the base or a great portion of the bladder into the wall of the rectum is practical, as it then becomes subject to the same internal tension as the rest of the intestine. This method is not difficult of accomplishment in the male.

Those operations in which the ureters are transplanted and have been preserved to their tips are correct only in principle if they are made after one of the methods which secures compression of the lumen.

The Coffey operation, practically a divided Martin, is accomplished by separating the ureters that have been isolated and brought through the posterior peritoneum, the distal ends being ligated and buried. A double-needled ligature is attached to the split ends of each ureter. At a point as low as convenient the sigmoid is held in a curved, rubber-covered clamp to protect against the discharge of intestinal contents. The bowel is then incised longitudinally for one and one-quarter inches through the peritoneum and muscularis, but not the mucosa; the mucosa is perforated at the lower end of the incision. The two needles are passed into the lumen of the bowel through the opening and out of its wall, slightly separated, one-half inch lower down, and are used to draw the ureter through the opening into the lumen, where

it is held by tying the two threads. The cut muscularis and peritoneum is now closed over the ureter in the incision by two rows of sutures (Fig. 129). The second ureter may now be attached or preferably the operation delayed for a later period. The Stiles operation (1907) and that of Mirotworzeff, which method is nearly the same and was reported in 1910, secure much the same effect by infolding the bowel over the ureter by numerous sutures, like a Witzel gastrostomy. The deflection of the ureters into the back,



Fig. 129.—Method of incorporating ureter into large bowel by the division of the peritoneum and the muscularis (after Coffey).

as described by Bottomley, is accomplished by a lateral incision, similar to that made in the extraperitoneal operation for stone in the ureter. The ureter is divided, the lower end ligated, and the proximal end brought out of the small incision posteriorly and an inch or more above the crest of the ilium, where it is sutured to the skin. This operation has been performed in our clinic from within the abdomen. If indicated at all, we consider this method more applicable for double tuberculous disease or advanced malignancy than to anastomose the ureters with the intestine. Should there

be a tendency to close, these openings can be maintained by the use of meatus dilators. Satisfactory urine collectors are easily adjusted by means of a belt (Fig. 130).

Concerning the dangers of necrosis of the ureters: The work of Margarucci, Monari, and also that of Kobylinski show that they may be freely separated for several inches without danger of necrosis if left free from tension.

In 1878 Smith transplanted the ureters into the colon in a case of exstrophy. He noted the intermittent peristaltic delivery of urine from the ureters, and Kelly has observed that when

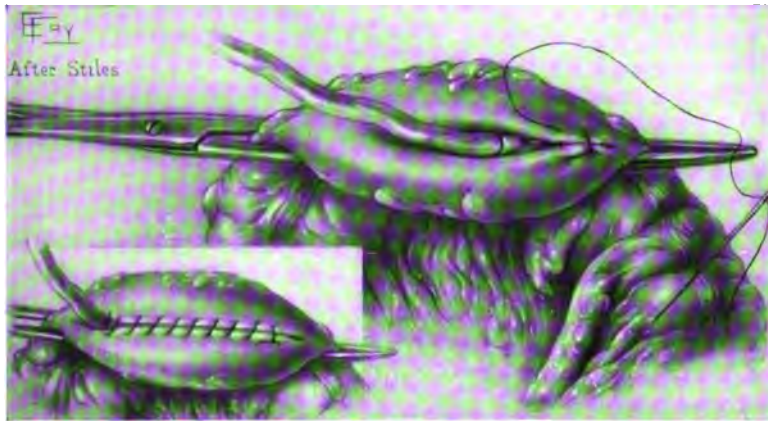


Fig. 130.—Infolded ureter in large bowel similar to Witzel gastrostomy (Stiles' method).

handled or irritated the peristalsis is stimulated. This point is of value in searching for the ureter within the abdomen. Scratching across the peritoneum over the supposed ureter proves it to be such if the peristaltic wave is seen, since the pelvic portion of the ureter is intimately attached to the posterior peritoneum, which should be remembered in locating them in low extraperitoneal operations.

In our cases of ureteral colonic implantation we have followed Stiles' plan of doing the operation in two stages, with an interval of from one to three weeks between. It has been our experience

that these operations are not satisfactory in children who are too young to attend to their own bowel movements. The control will be more difficult to secure primarily in these cases, and for a time they will require more frequent attention than before the operation.

Oppel's suggestion to try milk diet after Metchnikoff's plan of reducing the intestinal bacterial flora is undoubtedly a good one in the preparation of these patients. Oppel depends also on the functional test of the kidneys by giving a hypodermic of indigo-carmin, which he considers satisfactory if the urine shows blue in fifteen or twenty minutes. Phenolsulphonephthalein is used as a functional test of the kidney in cases examined in our clinic.

It is hardly necessary to state that the colon should be free from disease when anastomosing the ureters with it. Another point to be remembered in operations on the large bowel is that a laxative should be given two days preceding the operation in order that the contents may again become solid.

In the second group, or cases of injured ureters, it is often possible to implant the ureter into the bladder by the Coffey or Stiles method, a procedure we accomplished in 8 cases of cancer of the bladder involving one ureteral area. The cancers were removed transperitoneally, transplanting the ureters to the opposite side of the viscus while it was open. There were three cases of removal of the bladder for cancer. In one, a female, aged sixty-two, the ureters were transplanted into the rectum by the Stiles method. In spite of a defective kidney and dilated ureters there was a good operative recovery, but sudden death occurred some weeks later from cerebral hemorrhage. In one, a female aged twenty, the ureters were transplanted into the urethra by the Sonnenburg method. This patient made a primary recovery, and died one year later from acute infection of the kidneys. In the third case, a male, aged fifty, the bladder was removed transperitoneally, bringing the ureters into the back. This patient continues in good health, doing farm work for more than three years. In four cases of exstrophy of the bladder in which the organ was removed the ureters were transplanted into the rectum and lower sigmoid by



the Coffey method without mortality. Except in children, a day control of from three to five hours and an all-night retention may be obtained by this method.

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## CHRONIC CYSTIC MASTITIS\*

E. S. JUDD

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A difference of opinion still exists among the profession regarding the pathology of chronic cystic mastitis. This name was given to the process by Koenig, who, as the term implies, believed it to be one of chronic inflammation with cyst-formation. Other early observers, for example, Reclus and Schimmelbusch, believed that the cyst-formation and the cyst-degeneration, or the increase in the cellular elements, were the pathologic basis of the disease. Therefore, these authors have styled the condition "cystic disease of the breast" and "cystadenoma of the breast" respectively. Warren defines the process "abnormal involution," and Bloodgood defines it "senile atypical parenchymatous hypertrophy." These terms embrace the names of abnormal processes. However, it is not so important to have the process correctly named as it is that we should understand its relationship to cancer.

### TIME OF REAPPEARANCE AND PATHOLOGY

This type of chronic mastitis appears more frequently just before or during the menopause, in the period often spoken of as the "cancer age," that is, between the ages of thirty and sixty.

The pathologic picture of the condition varies so greatly that no fewer than 12 different descriptions have been published, each with a different name and each one describing a different arrangement of cells. The diversity of opinions on the pathology of these apparently similar conditions would lead us to believe that

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many of these pictures are different stages of one and the same process.

Various observers believe that chronic cystic mastitis is a precancerous stage, and that it often undergoes malignant degeneration (Koenig, Tietze, Keibel, Bloodgood, etc.). No one has as yet actually observed such development take place, though it is true that cancer is frequently seen in association with chronic cystic mastitis. MacCarty believes it is difficult to draw the line between the hyperplastic changes seen in chronic cystic mastitis and the pictures that are definitely cancer. He also believes there is no sharp line of differentiation, but that one condition merges into the other, and that cystic mastitis is usually, if not always, associated with cancer. He believes that the diagnosis can be made from the irregularity and characteristics of the cells, which, so far as can be determined, are exactly the same as the penetrating cancerous cells. The diagnosis of carcinoma should not always be postponed until the epithelial cells have penetrated the basement-membrane.

We are practically convinced that every case of cancer of the breast has associated with it some degree of chronic cystic mastitis, and it is most important to bear this point in mind, even though no definite relationship between the two has been demonstrated.

#### STATISTICS

Up to January 1, 1913, we had operated on 218 cases of chronic cystic mastitis. Of these, 11 were males, all occurring between the ages of twenty and thirty years. Two hundred and seven were females: Occurring between twenty and thirty years, 19; thirty and forty years, 63; forty and fifty years, 96; fifty and sixty years, 27; sixty and seventy years, 1; age not mentioned, 1. It will be seen that a large percentage of the cases occurred in patients between the ages of forty and fifty, and that nearly all occurred between the ages of thirty and sixty. Of the 218 cases, mastitis occurred 93 times in the right breast (5 males), 88 times in the left breast (5 males), and 30 times in both breasts. Six

were not mentioned. Of the 207 females, 140 had had children, 45 had no children, 3 had had miscarriages, and 22 not mentioned.

In reviewing the ages of the 711 patients with cancer, we find 79 per cent., or a large proportion of them, occurred in the "cancer



Fig. 131.—Incision for amputation of breast for chronic cystic mastitis. Incision extends onto the shoulder far enough to dissect flaps for axilla.

age," *i. e.*, between the ages of thirty and sixty. A large proportion occurred in the cases of chronic cystic mastitis, since during that same period (thirty to sixty years) there were 186 cases in the total 218 (85.3 per cent.).

### HISTORY AND PHYSICAL EXAMINATION

The greater number of patients gave a history of having had previous mastitis, and nearly all complained of pain. The pain which occurs with chronic mastitis is usually in the breast itself, does not radiate, and is associated oftentimes with soreness and

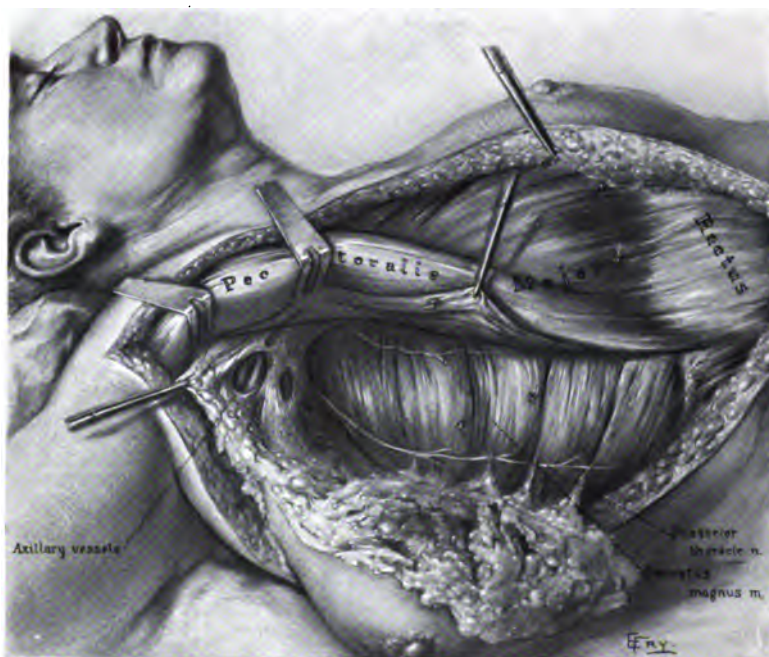


Fig. 132.—Showing pectoralis major preserved but reflected. Fascia has been dissected from muscles and the wall of the chest. Breast turned down, exposing axillary fascia and glands.

sensitiveness. It is often more marked during menstruation. The radiating pain complained of by the patients having cancer is entirely different in character.

On physical examination, if the breast is taken up between the thumb and forefinger, nodules can be distinctly felt, while if the hand is pressed flat against the breast and the breast compressed against the wall of the chest, these nodules cannot be

felt. Quite the opposite is true in cases of cancer, as many times the only way a small hard cancerous tumor can be palpated is by compressing the entire breast against the wall of the chest with the flat of the hand. If the breast be lifted up between the fingers, a small hard cancer lying embedded in the soft breast will often be missed. The individual nodules in mastitis are usually small

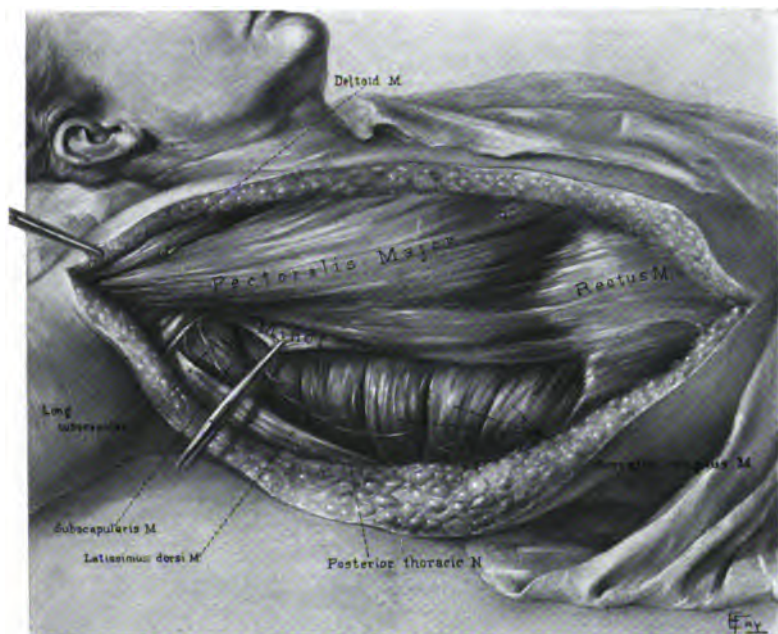


Fig. 133.—Showing axillary dissection completed; vessels and nerves exposed. Fascia from between pectoralis major and minor removed as completely as possible.

and very tense. Pressure on the breast will sometimes force a watery or dark fluid out of the nipple. The nipples may be slightly retracted, though the breasts are always freely movable on the muscles. The nodules of mastitis are freely movable in the tissue of the breast, and in this way differ from cancer, since the early process of malignancy, though having no attachment to the fascia of the muscle or skin, will show definite attachment to the sur-

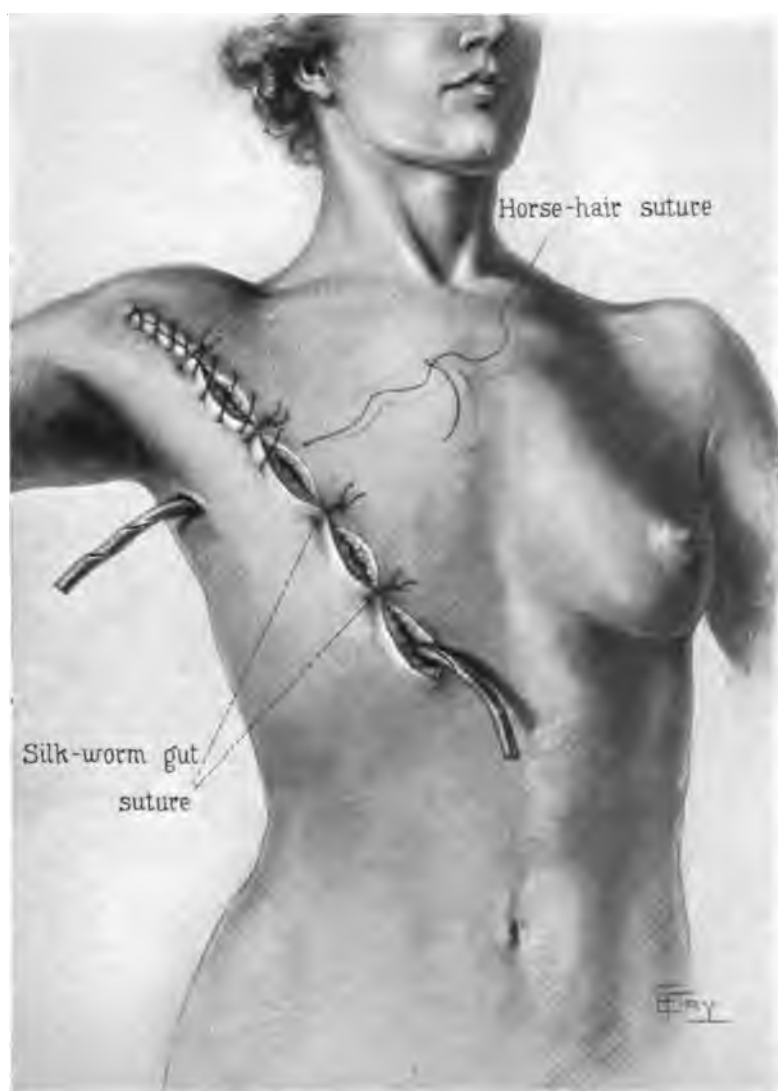


Fig. 134.—Showing closure of the incision, with two points of drainage, after the conservative operation.



rounding tissue of the breast. This attachment and infiltration about the tumor are characteristic of cancer.

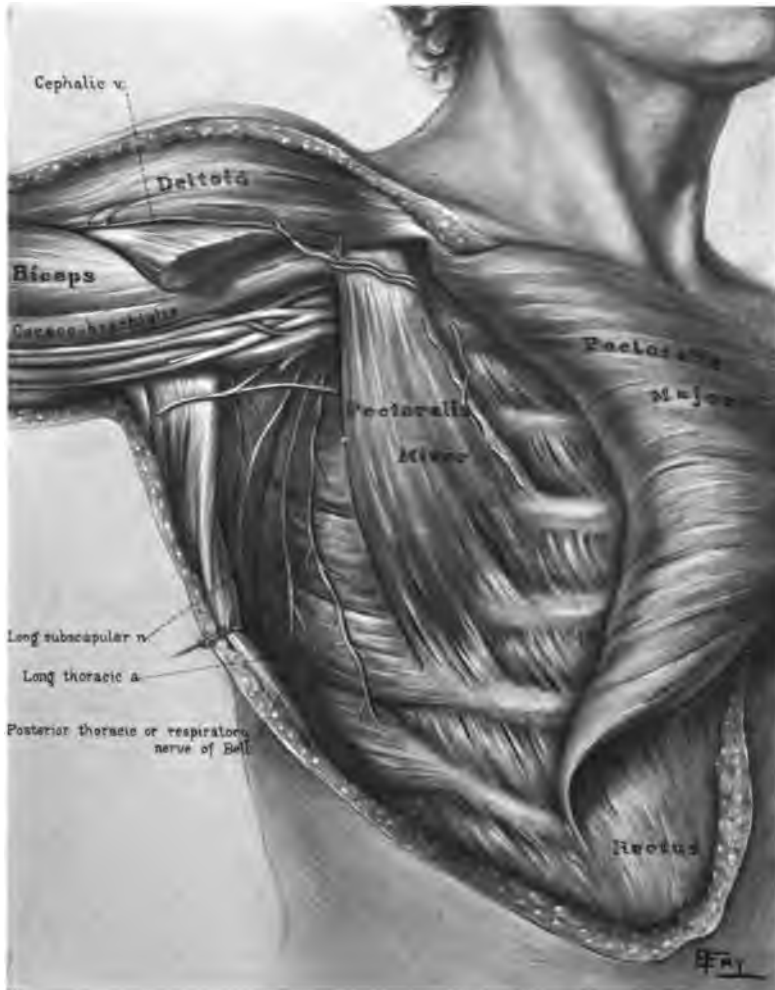


Fig. 135.—Anatomic dissection, showing the exposure of axilla, obtained by the more radical procedure of removal of muscles and fascia.

By keeping the clinical picture in mind and by a careful examination, we can make an accurate diagnosis of chronic cystic

mastitis in a large percentage of cases. In other words, as a result of our examinations we can tell these patients that they are suffering from chronic cystic mastitis, but we cannot tell them that the condition is not associated with an early cancerous process. This is particularly true if the patient consults us at an age when the condition is most likely to be malignant.

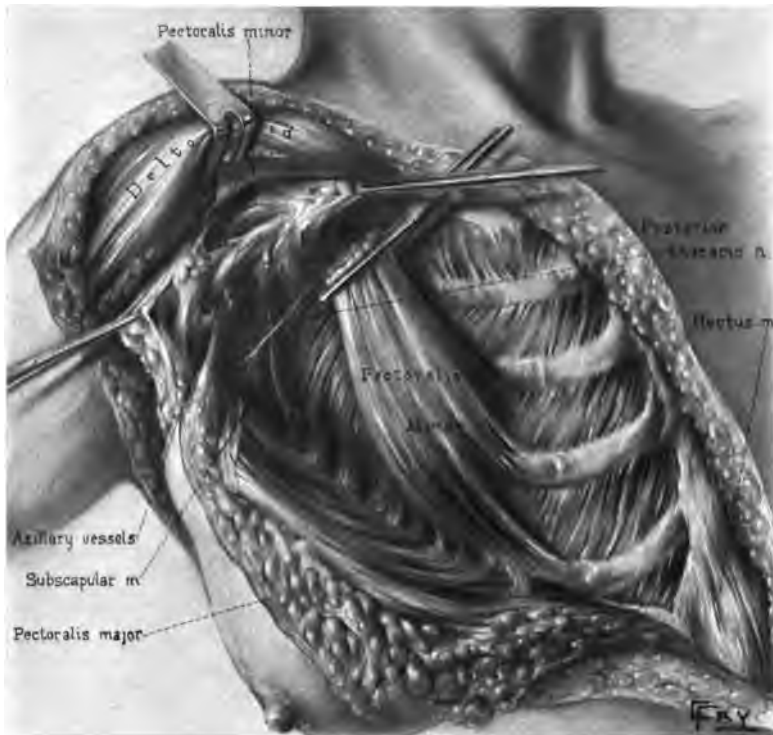


Fig. 136.—Shows pectoralis major, breast, and fascia turned down and insertion of pectoralis minor cut off from scapula. Fascia and glands lying underneath this part of pectoralis minor exposed.

Chronic mastitis in itself is benign, and except for its evident relationship to cancer and to relieve pain would require no treatment. The unsatisfactory results obtained in operating for well-defined cancer have led us to believe that progress in the surgical treatment of this disease will be made by operating in the pre-cancerous stage or at least in the very early cases.

## TREATMENT

For many years we realized that patients suffering from cancer did not come to the surgeon in time to be cured. Within the last few years, however, since the laity have become aware of the fact that early operations are successful, a noticeable change has taken

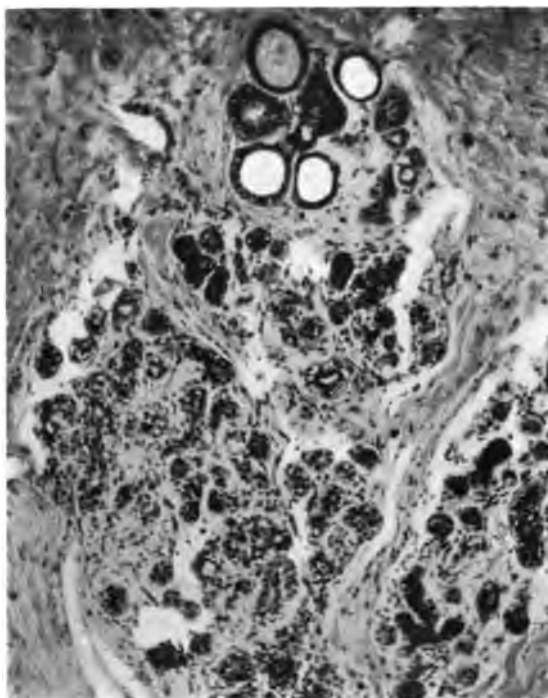


Fig. 137.—Showing almost normal breast tissue with few scattered round-cells and perhaps slight increase of fibrous tissue. Several slightly dilated acini show in left end of picture.

place in this respect. As Bloodgood has said, "This increases our responsibility greatly, because it is so much more difficult to recognize carcinoma in its early stages and because at this time we should be able to effect a cure in a large percentage of cases." Improved operative technic and more extensive procedures in advanced cases have failed to improve the results.

Knowing that practically every case of cancer of the breast has associated with it some degree of chronic cystic mastitis, and that many of the best authorities believe the condition occurring in women of the cancer age will become malignant in more than half the cases, we conclude that this condition in all



Fig. 138.—Showing cystic mastitis with desquamation of inner row of cells in acini and great increase of fibrous tissue.

probability is often a precancerous stage, and that it should be treated as such.

Cancer of the breast has not been observed in the young person under twenty-seven years of age having a bilateral painful mastitis. Cancer in these young individuals usually occurs as a solitary nodule, and more often as a degenerating fibro-adenoma. Young individuals with diffuse, painful, nodular enlargement of

both breasts should not be operated on unless a recent change has occurred in some one of the nodules, and then this nodule should be excised for microscopic diagnosis before doing a radical operation.

In view of the fact that medical treatment oftentimes does not relieve these patients, it may occasionally be deemed advisable

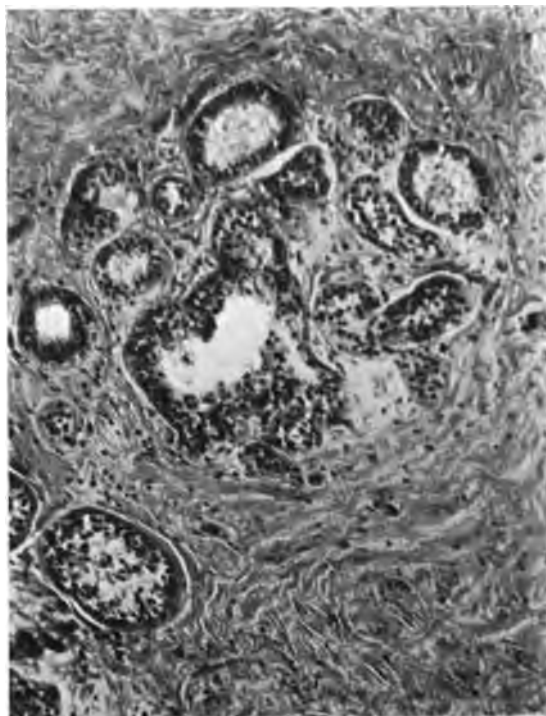


Fig. 139.—Schimmelbusch's disease; abnormal involution or senile parenchymatous hypertrophy; adenocystic disease; marked increase of cellular element and of fibrous tissue.

to excise a piece of the breast, preferably by the Warren operation, to relieve their suffering. The result is apt to be rather unsatisfactory, since other nodules may develop and take on the same symptoms. Occasionally it may be necessary to amputate the entire breast because of pain.

Our responsibility would seem to be greater in regard to those

patients coming to us between the ages of thirty and forty. While cancer is not common at this time, yet it occurs in a considerable percentage of the cases. A radical operation for all is the surest method, but in doing this we would undoubtedly operate on many unnecessarily, removing the breast at a time when it is functionally active. It would seem a better procedure in these cases to remove

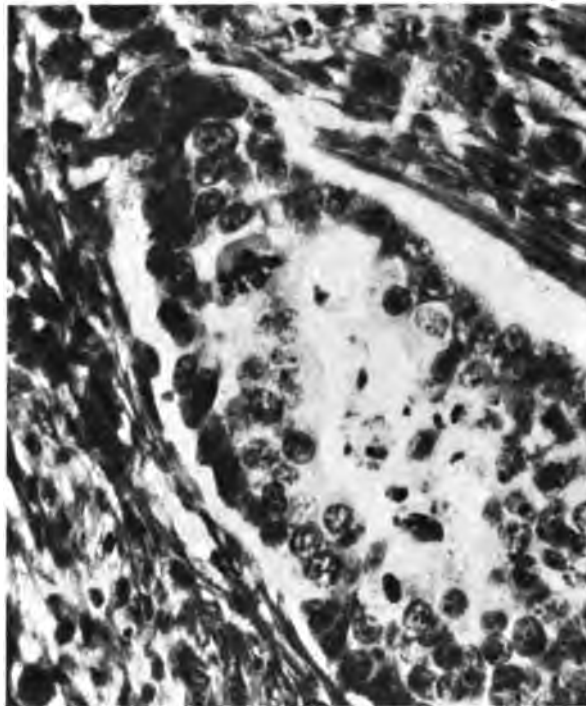


Fig. 140.—Same under high power, showing a single acinus with cells enlarged. Several karyokinetic figures show, and in the center, some destroyed cells.

for microscopic investigation the part of the breast which appeared most affected, and abide by the pathologist's diagnosis, doing a radical operation at the time if necessary. We have followed this plan for many years in several hundred operations on the breast. In only one instance was the cancer missed. This was a case of double suppurative mastitis in a lactating breast; cancer was

not suspected nor diagnosed, probably because no part of the malignant tissue happened to be removed. A radical operation was contraindicated because of the existing infection and sloughing, which incurred considerable risk and promised little or nothing at a time when the gland was lactating and physiologically active. The radical operation has been performed several times when

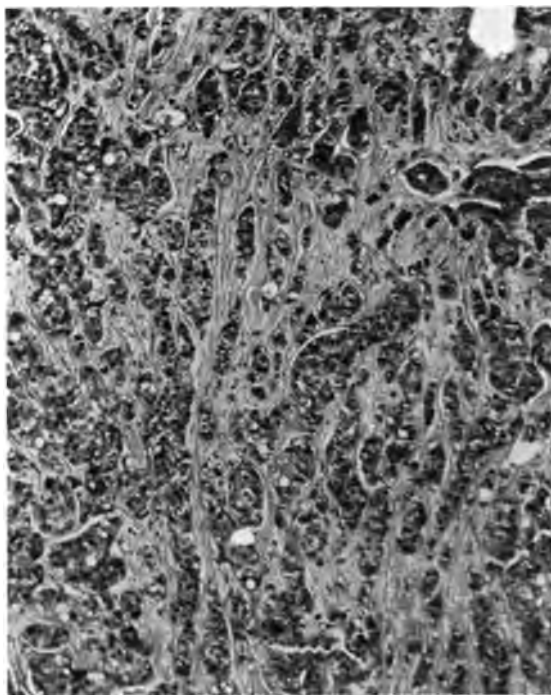


Fig. 141.—Typical carcinoma. Rows of carcinoma cells. Much increase of fibrous tissue.

there was doubt in the pathologist's mind as to whether or not the specimen was malignant, and it would seem to be the advisable procedure in doubtful cases.

In patients between the ages of forty and sixty our responsibility is perhaps somewhat lessened, since at this time the important function of the breast has ceased and also we have good authority for believing that a certain percentage of the cases change

to malignancy. Chronic cystic mastitis can usually be definitely diagnosed clinically during this period.

Several conditions must be taken into consideration regarding the treatment of this disease when it occurs between the ages of forty and sixty years: (1) Cystic mastitis is associated with definite malignancy; (2) the mastitis is definite, but the malignancy is uncertain; in either case it would seem best to perform the radical operation for cancer; (3) chronic cystic mastitis in which the pathologists are unable to define malignancy and in which there are no areas suspicious of cancer. In this case we realize that we are dealing with a condition usually associated with cancer, and yet, according to the present status of pathologic knowledge, it is not malignant. A partial amputation of the breast in these cases will not relieve, and in many instances the same process will start up in the remainder of the gland—for this reason the entire gland should be removed. The axillary fascia with the glands can be removed without additional risk or inconvenience to the patient, and this should be done, since it is the avenue traversed by cancer-cells. Removing the muscles, as is done in operating for cancer, is a more severe procedure, and more difficulties occur during convalescence. At times permanent limitations of motion and swelling in the shoulder and arm occur, and while this interference with function should not be considered in operating on the malignant case, it would seem best to give it due consideration in definite benign conditions.

In 211 of our 218 cases the conservative operation was performed, and in none of the cases has there been evidence of malignancy afterward. In the remaining 7 cases of doubtful malignancy the radical operation was performed.

#### CONCLUSIONS

In conclusion it may be said: (1) I believe chronic cystic mastitis has a definite relationship to cancer of the breast and in many instances may be considered a precancerous condition. (2) In cases suspicious as to malignancy a radical operation for cancer should be performed. (3) In cases of chronic cystic mastitis that



cannot either clinically nor pathologically be diagnosed as to malignancy, the conservative amputation with removal of the gland-bearing fascia is the operation of choice.

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## HISTOGENESIS OF CARCINOMA IN OVARIAN SIMPLE CYSTS AND CYSTADENOMA

WILLIAM CARPENTER MACCARTY

The apparent histogenesis of mammary carcinoma\* from the stratum germinativum of the mammary gland has stimulated further investigation of other organs. The ovary which the surgeon removes for many conditions, such as acute and chronic oöphoritis, the latter condition especially in association with hysterectomies for large fibroids and uterine carcinoma, and the apparent varieties of cystic and solid neoplastic conditions, is a fruitful field for the study of epithelial activities. This is especially true because one sees cysts which vary greatly in size and frequently far exceed those which are found in the breast.

\* In an examination of 1000 mammary pathologic conditions it was found that the cells which are the direct progenitors of the carcinoma cell were those which lie beneath the differentiated or functionating mammary epithelium. These germinative cells are almost invisible in the normal breast, and are to be seen to best advantage only in conditions in which there is a demand made for the replacement of differentiated cells. In chronic mastitis one sees exfoliation and necrosis of the functionating cells, plus hypertrophy and hyperplasia of the germinative cells. The latter do not resemble the differentiated cells in that they are round, have clear protoplasm and faintly staining nuclei. The epithelial hyperplasia of the germinative cells in the breast may be divided into three definite histologic pictures.

Primary hyperplasia is seen in the presence of two rows of cells, the differentiated mammary cells resting upon a row of partially differentiated cells which are germinative cells of the differentiated cells. Both rows are present.

Secondary hyperplasia may be seen after the complete exfoliation of the differentiated cells. The partially differentiated cells grow into the lumen of the acinus, and are not differentiated to resemble functionating cells.

In tertiary hyperplasia the germinative cells not only grow as undifferentiated cells into the lumen, but invade the stroma, thereby producing the picture which is recognized in carcinoma.

MacCarty: "The Histogenesis of Carcinoma of the Breast," Surg., Gyn. and Obst., October, 1913; also Collected Papers, Mayo Clinic, 1913.

MacCarty: "Carcinoma of the Breast," Trans. Southern Surg. and Gyn. Soc., 1910; also Collected Papers, Mayo Clinic, 1911.

The material under investigation consisted of 1000 specimens. These represented practically all the pathologic conditions which

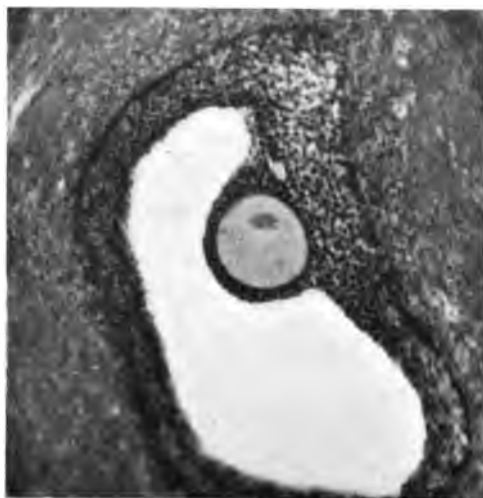


Fig. 142.—Normal Graafian follicle.



Fig. 143.—The lining epithelium of a Graafian follicle, showing the stratum germinativum or basal layer of the epithelium.

one finds recorded, and consisted of inflammatory conditions, benign and malignant, solid and cystic tumors.

The specimens were studied both in the fresh and fixed conditions in a similar manner to that which was employed in studying

the breasts, with the exception that many of the smaller cysts were embedded in celloidin, in order more perfectly to retain their contour.

In order more clearly to understand the probable relation which exists between the cystic ovarian anatomic unit, namely, the Graafian follicle, the corpus luteum, and pathologic cystic conditions, a series of apparently "normal" ovaries which were obtained at autopsy were utilized.

Beginning, therefore, with the simplest normal condition in the ovary one finds the Graafian follicle, which is structurally

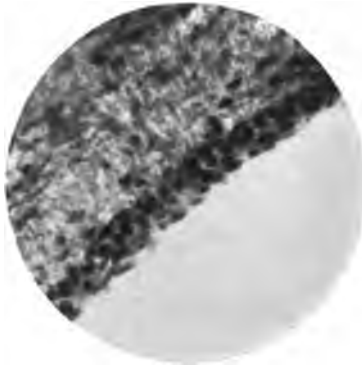


Fig. 144.—Lining epithelium of a large Graafian follicle or a small simple ovarian cyst.

and physiologically a small cyst, lined by many layers of epithelial cells with small oval nuclei (Figs. 142 and 143). The ovum is embedded in a local proliferation of this epithelium. The arrangement of the "basal" epithelium which rests upon the stroma suggests the arrangement of the "stratum germinativum"\* of the skin and of the breast (Fig. 157). Fig. 144 was made from a section through the wall of a cyst, which may be a large Graafian follicle or a small ovarian cyst.

\* This term has been given by embryologists to the regular layer of epithelium of the skin which lies immediately adjacent to the stroma, the layer from which the epidermis is differentiated. An extensive list of literature may be found appended to "The Histogenesis of Carcinoma of the Breast," Surg., Gyn. and Obst., October, 1913 (MacCarty).

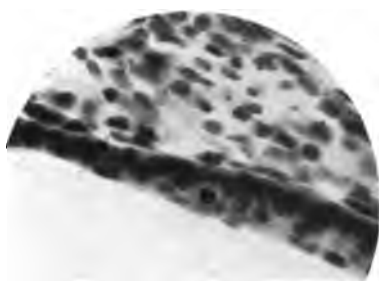


Fig. 145.

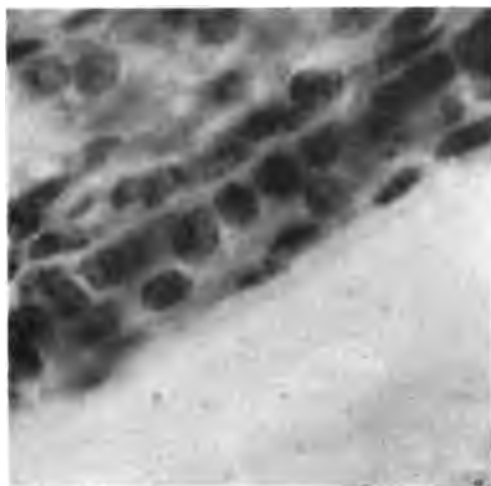


Fig. 146.

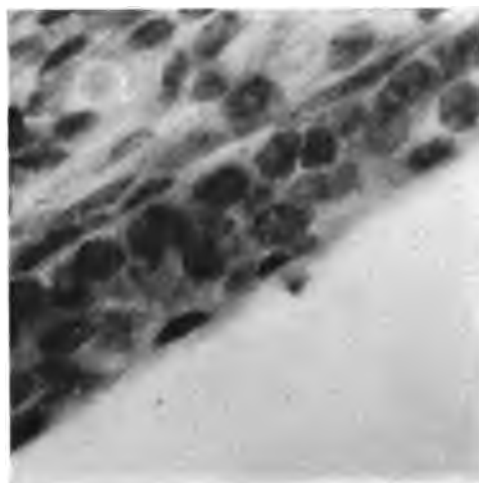


Fig. 147.

Figs. 145, 146, and 147.—Irregular hyperplasia of the cells of the stratum germinativum of the lining epithelium of a simple ovarian cyst (primary hyperplasia).

The type of the epithelium of a simple cyst is indistinguishable from that in the Graafian follicle.

At this point it may be well to describe a series of pictures



Fig. 148.—The cuboid or columnar epithelium of an ovarian cystadenoma (secondary hyperplasia).

which anticipate a discussion of the probable gradual evolution of the epithelium of cystadenomas and ovarian carcinomas. In Figs. 154, 155, 156, one sees three different “types” of epithelium



Fig. 149.—Hyperplastic epithelium lining a cyst of an ovarian cystadenoma (secondary hyperplasia).

in one small cyst, the oval cells of the simple cyst, and the columnar epithelium of the cystadenoma and papillary cystadenoma.

The presence of these so-called types of epithelium in a single

small cyst, which is less than 3 mm. in diameter, may more readily make clear the relation which probably exists between the epithelium in typical Graafian follicles, simple cysts, and cystadenoma. In Figs. 145, 146, and 147, one sees the irregular epithelial hyperplasia of the cells of the stratum germinativum in a simple cyst. In Fig. 148 one finds the typical lining of a cystadenoma. The cells bear apparently the same morphologic relation to the stratum germinativum of the epithelium of the follicle that the hyperplastic outer row of cells of mammary acini (Figs. 157, 158, 159, 160) bear to the conditions, which are described in the breast

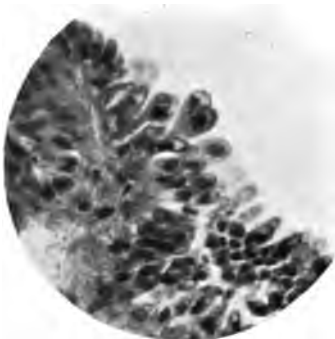


Fig. 150.

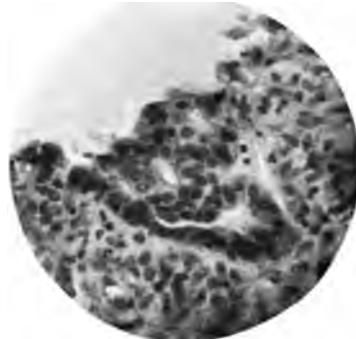


Fig. 151.

Figs. 150 and 151.—Hyperplastic epithelium lining an ovarian cystadenoma, plus invasion of the stroma by the epithelium (tertiary or migratory hyperplasia).

as cystadenoma. This condition, when present alone, may be described as secondary hyperplasia.\*

Figs. 148 and 149 show hyperplastic epithelium in the wall of

\* As a result of the non-descriptive terminology which has been given to pathologic conditions in the breast, especially the so-called varieties of carcinoma, and on account of the chaotic condition which has arisen in the minds of surgeons and, indeed, pathologists relative to the actual activities of the epithelium in the breast, the writer has described the morphologic evidences of these activities in the terms of hyperplasia.

This term has biologic significance; it has definite descriptive value, and represents activity, which is the fundamental thing from which prognosis is to be studied. Instead of the numerous synonyms and semi-scientific, non-descriptive terminology which exists in the literature, it seems that the adoption of simple biologic terminology may place material in a condition to be more correctly correlated with clinical data.

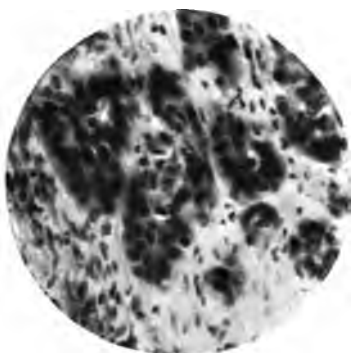


Fig. 152.

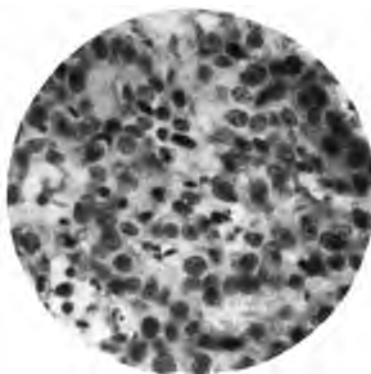


Fig. 153.

Figs. 152 and 153.—Tertiary or migratory hyperplasia in an ovarian cystadenoma.

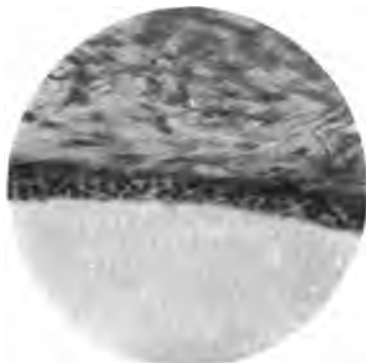


Fig 154.



Fig. 155.



Fig. 156.

Figs. 154, 155, and 156.—Different parts of the lining epithelium of an ovarian cyst 3 mm. in diameter.



a large typical ovarian cystadenoma. The cells have lost their typical columnar shape, although here and there columnar cells may still be seen. In a similar manner to the behavior of the hyperplastic outer row of cells in the breast one finds that the line of demarcation between the epithelium and the stroma is less definite.

Figs. 150 and 151 show the absence of the line of demarcation and the presence of invasion of the surrounding stroma.

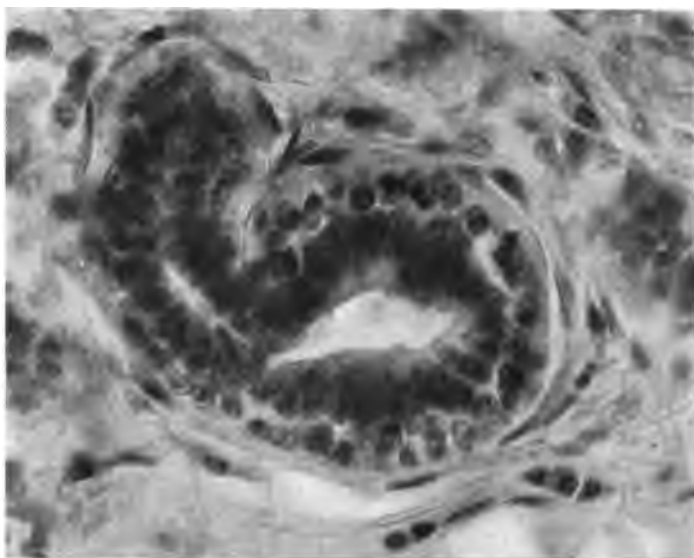


Fig. 157.—A mammary acinus showing the cells of the stratum germinativum and the differentiated cells (inner row) (primary hyperplasia).

Figs. 152 and 153 show the cells which have invaded the stroma of the ovary. They present a typical picture of adenocarcinoma.

During the study of this material the facts which have been pictorially presented here were noteworthy, especially in the light of the behavior of epithelium in the breast under abnormal conditions. The conditions have been studied and published in the literature in the term of entities, just as in the breast. The same process of evolution, however, suggests itself to the writer, and

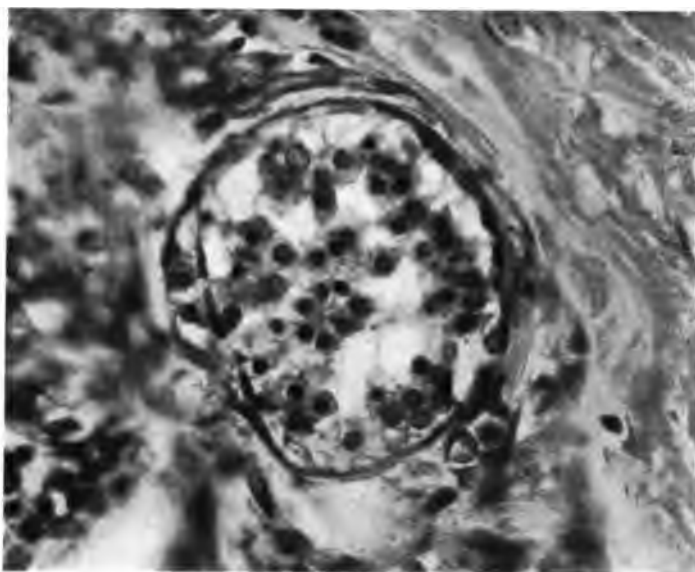


Fig. 158.—Hyperplasia of the outer row of cells of a mammary acinus after the disappearance of the differentiated cells (secondary hyperplasia).

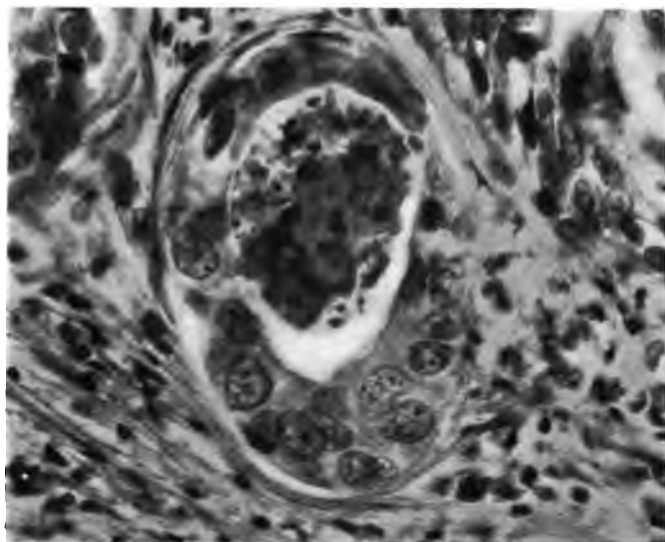
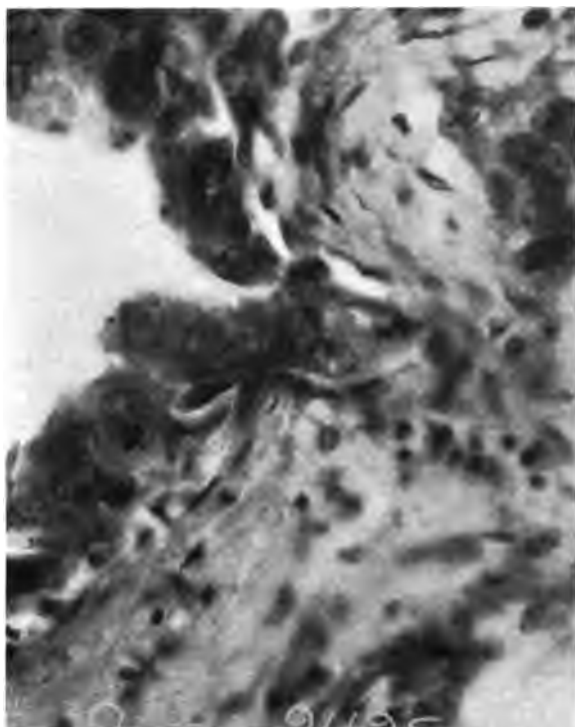
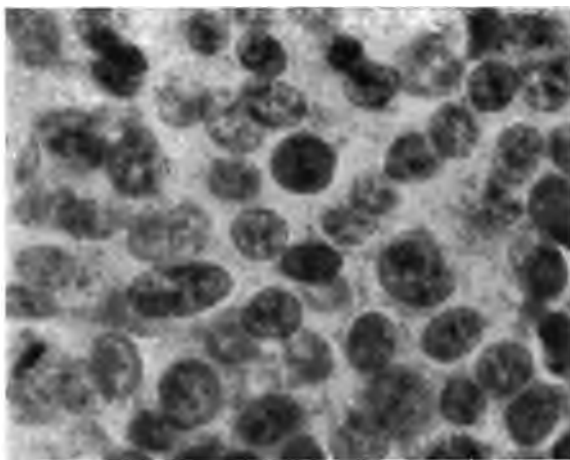


Fig. 159.—Secondary hyperplasia in a mammary acinus, showing the irregularity of the nuclei.



**Fig. 160.—Tertiary or migratory hyperplasia in a mammary acinus, showing the local indistinctness of the line of demarcation between the intra-acinar cells and the stroma.**



**Fig. 161.—Tertiary hyperplasia of the breast.**

terminology relative to the epithelium may be also applied accordingly. When the differentiated epithelium of the Graafian follicle and the simple cyst are found, the condition may be spoken of as *primary hyperplasia* (Figs. 142, 143). When the differentiated cells are absent and have been replaced by less differentiated cells of the so-called "outer row" or "germinative row" of cells, one may describe the condition as *secondary hyperplasia* (Figs. 148 and 149).

When the cells of this secondary hypertrophic and hyperplastic layer have obliterated the distinctness of the demarcation between themselves and the stroma and have invaded the underlying tissue, one may speak of a *tertiary hyperplasia* (Figs. 150, 151), or migratory hyperplasia.

Recognition of these conditions and the applications of such terms as primary, secondary, and tertiary do not mean that these conditions must always pass through these stages in all cases. Indeed, nothing is said relative to whether or not the conditions are necessarily sequential.

The conditions which have been briefly presented indicate, in the light of findings in the mammary gland, that there is a possibility that the histologic similarity which exists between various stages of epithelial hyperplasia in Graafian follicles, simple cyst, and cystadenomas and carcinoma of the ovary may not only be similar, but represent actual stages which may be occasionally sequential, as is the case in the breast.

The links in the chain of evidence which are presented here may assist others more clearly to demonstrate the evolution of carcinoma in the ovary in a similar manner to that which has been demonstrated in the mammary gland.

## END-RESULTS IN OPERATIONS FOR CANCER OF THE BREAST\*

E. S. JUDD, ASSISTED BY W. E. SISTRUNK

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The following is a review of the results of operations in our clinic for cancer of the breast from January 1, 1902, to January 1, 1912.† It was originally intended to report all the cases of mammary cancer that had been operated on more than three years, but in spite of the fact that we have endeavored, for several years, through correspondence and personal communication, to complete our post-operative records, so far accurate data in many of the earlier cases have not been obtained. It seems best, therefore, to make this report cover the results of the ten consecutive years up to two years ago, of which we have fairly correct knowledge, hoping to be able to complete the data on the earlier cases at some future time.

Previously it was customary to allow three years to elapse before making claims of a cure following an operation for cancer. It is undoubtedly true that many patients who pass through the first three years without recurrences do remain well, but it is also true that a certain percentage of them have recurrences and metastases at a period much later than three years. In view of this it is difficult to say how much time should elapse before a patient operated on for mammary cancer may be said to be cured.

It is impossible to state what course these cases would have taken had they not been operated on, but, judging from the histories of similar though non-operated cases, it is fair to assume

\* Read before the Southern Surg. and Gyn. Assoc., Atlanta, December 16-18, 1913. Reprinted from *Surgery, Gynecology and Obstetrics*, 1914, vol. xviii.

† These operations were performed by C. H. Mayo, E. H. Beckman, E. S. Judd, and D. C. Balfour.

that a goodly proportion of those operated on reasonably early have been either cured or at least have had an extension of life and a comfortable existence for many years. "Cases not operated on prove fatal on an average in twenty to twenty-eight months, the extremes varying from less than two months to more than twenty years" (Finney).

The cases upon which our study is based are consecutive cases, and none has been omitted from which post-operative data were obtained. Many operations were known at the time to be palliative, and were performed because of ulceration or the patient's extreme suffering. Many times these palliative operations were satisfactory, bringing relief and apparently prolonging life.

The principle in the technic of all the radical operations was practically the same, and consisted in the removal of the entire breast, axillary glands, and fascia, including the pectoralis major and minor muscles in every case. These structures were usually all removed in one piece. In the evolution of the operation the tendency in the later years has been to remove more widely the subcutaneous and deep fascia in all directions. In some cases it has been necessary to skin-graft the wound in order to close it, though in most of our cases we have been able to suture the skin-flaps directly. In many of the cases we employed technic as suggested by Jackson and also by Rodman, and have found their methods very useful.

It has not been our practice to remove the fascia and glands from above the clavicle. If these glands are palpable, one is removed for microscopic examination to determine the nature of the enlargement. If the supraclavicular glands prove to be involved, it has usually been our experience that the individual lives longer and more comfortably if not operated on. In some cases, however, especially when the lesion in the breast is in one of the upper quadrants, and especially if there be attachment to the skin, we believe that it is advisable to continue the dissection of the fascia and glands to the supraclavicular region. In most cases in which the glands were involved the individual has not lived three years. In one of such cases, however, the glands

showed definite cancer and the patient is now living (more than five years) without recurrence.

The diagnoses in all these cases were made from both macroscopic and microscopic evidence. During the ten years from January 1, 1902, to January 1, 1912, we have operated on 609 patients with cancer of the breast. Of these, 607 were females and 2 were males. One of the males is alive without recurrence three years following the operation. The other male died at the end of two years and eight months from recurrence.

Of the 609 cases, we have been able to trace and have fairly accurate knowledge of 514. No patients in this series died in the hospital, though three died within one month after the operation. Patient No. A7541 died at the end of two weeks, when the wound was well healed; the autopsy in this case showed a large pulmonary embolism as the cause of death. Patient No. A46874 died at the end of the fourth week in diabetic coma. The wound had healed and the autopsy showed no carcinoma. In patient No. A22134 the wound did not heal, and the patient developed septic phlebitis, dying at the end of the fourth week from sepsis.

In estimating the age incidence of carcinoma of the breast we found that the youngest patient was twenty-five and the oldest eighty-five years of age. Estimating the number of cases occurring in each decad we find:

20 to 30 years of age	13 patients
30 to 40 " " "	147 "
40 to 50 " " "	228 "
50 to 60 " " "	147 "
60 to 70 " " "	88 "
70 to 80 " " "	27 "
80 to 90 " " "	1 patient

In one patient, twenty-six years of age, a tumor in the lower inner quadrant of the right breast was supposed to be benign, but at the time of removal it proved to be cancer. The wound was packed with gauze saturated with Harrington's solution, and two days later a radical operation was performed. This patient is alive and without recurrence seven years and nine months after operation.

One patient, twenty-five years of age, whose tumor was diagnosed as malignant intracystic papilloma, at the time of the operation was nursing a nine-months-old baby. She is alive without recurrence more than six years.

One patient, twenty-eight years of age, with carcinoma of the left breast and concerning whom the prognosis at the time of operation was considered to be good, except for her age, is well now after three years and three months.

One patient, twenty-six years of age, diagnosed as early cancer of left breast, is alive with questionable local recurrence two years and nine months after operation.

One patient, twenty-eight years of age, with cancer of the right breast and axillary glands, recurring after a partial removal of the breast elsewhere one year before, is alive without recurrence two years and nine months after operation.

These cases are mentioned especially to show that mammary cancer in a young person is not necessarily hopeless, and that a good percentage of the cases coming for treatment early may be relieved for a long time, and that even in recurring cases a fair result may sometimes be obtained.

As will be seen from the table, many of our cases have occurred in the so-called cancer age,—forty to fifty years,—and by far the greatest proportion between thirty and sixty years. Nearly all the younger patients who remained well have been those who came for treatment early before there was any evidence of extension to the lymphatics.

In Table I may be seen the percentage of cases for each decade who have died within the first year after operation. We cannot explain why the younger patients have apparently done better than the older ones, except that the great majority of these cases come for treatment early.

Of the 514 patients whom we have been able to trace, 266, or 51.7 per cent., are known to be dead. Twenty-one of these died from other causes without clinical signs of recurrence. On several of these patients autopsies were performed and no recurrence was found. Subtracting these from the number who have died from



cancer, leaves 47.6 per cent. of deaths from cancer for the entire series. Of the 514 patients, 248 are known to be alive from two to eleven years and four months. Thirty-seven of these living are known to have recurrences.

TABLE I.—PERCENTAGE OF DEATHS ACCORDING TO AGES

BASED ON NUMBER OF PATIENTS HEARD FROM						
	AGES	Died Within One Year	Died Within Three Years	Died Within Five Years	Died After Five Years	Alive Two to Ten Years
	20-30	0	0	0	0	5 patients
Total preclimac-	30-40	20%	46%	55%	1%	49%
teric periods . . . . .		19%	43%	52%	1%	47%
	40-50	20%	45%	50%	5%	43%
Total climacteric	50-60	16%	45%	57%	1.8%	41%
periods . . . . .		19%	45%	53%	4%	42%
	60-70	16%	37%	44%	7%	48%
Total postclimac-	70-80	7%	50%	50%	7%	43%
teric periods . . . . .	80-90	0	0	0	0	1 patient
		13%	39%	45%	7%	48%

TABLE II.—RESULTS IN PATIENTS OPERATED ON OVER PERIODS OF THREE YEARS

510 patients operated on more than three years.  
 427 patients have been traced.  
 234 patients have died.  
 191 patients are living.

44.7 per cent. of patients have lived more than three years.  
 27 of these patients have recurrence at the present time.  
 19 patients died from other causes.

In 1902, 24 patients were operated on. Of these operated on more than eleven years, we have traced 19: 15 have died from various causes, and 4 are alive and have no recurrence. Thus, 21 per cent. of this series are now alive, over eleven years, and without recurrence. In each of these patients the carcinoma was in the left breast. The axillary glands were enlarged in two of them. One of this series who died had had a fairly radical operation elsewhere twelve years before. She came to us with recurrence in the skin and axilla. This was removed, and she lived two

years and two months following this operation. One of these early patients lived six years and nine months after the operation, and died of arteriosclerosis without evidence of recurrence. One other lived six years without local recurrence and died of metastases in the liver.

Twenty-six patients were operated on in 1903. Of these, we have been able to trace 21. Of this group of 21, 43 per cent. are alive without recurrence. All these patients have lived more than ten years. Two in this series had been operated on for malignant disease in other organs. One patient had had a hysterectomy for carcinoma of the uterus two years before, and one other had been operated on three months before for malignant papillary ovarian cysts.

*Patients Living More Than Ten Years.*—Of the patients operated on during the years 1902 and 1903, we have been able to trace 40. Twenty-seven are known to be dead from various causes, which leaves a percentage of 32.5 alive without recurrence more than ten years. Three of the patients who died lived more than six years and died from other causes.

*Patients Living More Than Five Years.*—Of the 321 patients operated on more than five years, 266 have been traced. Of these, 148 are known to be dead; 106 are living, thus giving a percentage of 39.8 who have lived more than five years. Six of these patients have recurrence at the present time. Fourteen included in these deaths have died from other causes.

*Patients Living More Than Three Years.*—Five hundred and ten patients have been operated on more than three years, 427 of whom have been traced. Two hundred and thirty-four are dead, 191 are living, leaving a percentage of 44.7 of patients living more than three years. Twenty-seven of these have recurrences at the present time. Nineteen are known to have died from other causes.

*Late Recurrences.*—We have also in this series several who have died from carcinoma after being free from it for a number of years. In one instance the patient died nine years and one month after the operation from general carcinosis. One had metastases

in the lungs five years and eleven months after operation. One had internal metastases in the liver six years and four months; another had metastases without any local recurrence and died six years and five months after operation. In one instance we operated for recurrence twelve years after the primary operation, the patient remaining well nearly three years after the secondary operation.

We have known for some time that late recurrences occur following operations for carcinoma of the breast, but we have been rather surprised to find so many patients with late recurrence. In reviewing the literature on this subject we have found one case reported by Matas with recurrence nearly twenty-five years after the first operation; and another reported by Ransohoff in which there was recurrence nearly twenty years after the primary operation.

Our statistics do not bear out the supposition that excision of the tumor or a part of the breast, followed by a radical operation within a few days or weeks, means always a bad prognosis. For example, in one of our cases the breast was removed for supposed mastitis. This was found on examination in the laboratory to be carcinoma. It is our custom in such cases to arrange for an immediate radical operation in all instances if it is found to be necessary. In this particular instance, however, the radical operation was not performed until seventeen days after the incomplete operation. This patient is now living without signs of recurrence seven years and nine months after the operation. In another case a specimen had been removed one week before the patient came to our clinic, and at operation definite carcinoma of the breast was demonstrated. This patient at the present time is alive and free from recurrence six years and two months after the operation. In one other case which is still more striking the patient's breast was removed elsewhere four years before. Some weeks after this operation she developed nodules in the axilla. These were treated by x-ray over a period of some months. We removed the recurrent masses, and she has been living now six years and six months without further evidence of cancer.

On the other hand, we have had five cases in this series in which specimens had been removed elsewhere from three weeks to one year before our radical operation, and all these patients died from two months to two and one-half years later.

We have had several patients in whom both breasts were involved. If both were involved at the same time, the prognosis, as a rule, was bad. If one had been removed and there was later recurrence in the other breast, the prognosis was often quite favorable. In 1905 we operated on a patient whose opposite breast had been removed in 1899. She lived four years and eight months after the second operation.

In 1906 we operated on two patients in whom there was a very small lesion in the breast and no glandular involvement could be found. Macroscopically and microscopically the diagnosis was early carcinoma and we believed both were favorable cases. Both of these patients had early metastases and one died within two years. These two patients seem to illustrate a certain group who in all probability, at the time of operation, have internal metastases or extension to the mediastinal glands without evidences of such extension. We have seen several hopeless cases because of metastases to the liver, spine, or bones, and yet in which the primary focus was small and free and no enlarged glands could be felt. We have also observed two such patients with pathologic fractures of the femur. In both of these the fractures occurred five years after the operation. Metastasis to the bones has not been common, though many of the replies to our inquiries would indicate involvement of the vertebræ. Involvement of bone is usually late.

We have considered edema in the tissues as a contraindication to operating, because we believed that the lymphatics were all blocked by the extension of the cancer. One of these patients in whom the prognosis was bad because of edema and who was operated on as a palliative measure is yet alive without recurrence five and one-fourth years later. Cancer in the lactating breast has been most unfavorable. Of the 3 patients operated on, 2 have died within the first year; in the one exception the growth was an intracystic papilloma.

*Functional Result.*—Special inquiry has been made regarding the ability to use the arm and shoulder following these operations, and a very large percentage of the patients have reported that their arms are all right or practically as good as ever. We have noticed that when it is necessary to destroy one of the motor nerves the function is much more apt to be impaired. Pain in the arm is usually complained of shortly after operation, but in most of our cases this entirely disappears within two weeks. We have made special inquiry regarding edema in the arm. Occasionally the swelling and edema have been marked. Counting the patients with the edema and those who say they have some swelling of the arm at times, the entire group is not over 5 per cent. The edema, as we have seen it, occurs in two ways: first, as primary edema immediately following the operation. This is quite common, and we believe it is due to a thorough removal of the lymphatics; it persists until collateral circulation in the lymphatics has been established. This is usually a matter of two or three weeks and can be relieved by early exercise and massage. Second are those patients in whom the edema comes on late—several months or years after the operation. Here it is due to a recurrence of the carcinoma in the remaining lymphatics which have been draining the arm, and, of course, is permanent. In four patients we have removed the entire axillary vein down to the cephalic vein, taking care that the latter was not injured. The resulting edema was but slight and temporary. Even with the removal of the pectoral muscles, intercostals, part of the latissimus dorsi and serratus magnus, and all the axillary fascia and lymphatics, in many of these cases the function of the arm and shoulder has been impaired very little.

TABLE III.—RESULTS IN PATIENTS OPERATED ON OVER PERIODS OF FIVE YEARS

321 patients operated on more than five years.

266 patients have been traced.

148 patients have died.

106 patients are living.

39.8 per cent. of patients have lived more than five years.

6 of these patients have recurrence at present time.

14 of these patients died from other causes.

TABLE IV.—RESULTS IN PATIENTS OPERATED ON OVER PERIODS OF TEN YEARS

50 patients operated on more than ten years.  
 40 patients have been traced.  
 27 patients have died.  
 13 patients are living.

32.5 per cent. of patients have lived more than ten years.  
 None of these patients have recurrence at the present time.  
 3 patients died from other causes.  
 All these (3) patients lived more than six years.

TABLE V.—NUMBER OF CASES AND PERCENTAGES FOR EACH YEAR

YEAR	NO. OF CASES	TRACED	DEAD	ALIVE, NO RE- CURRENCE	ALIVE WITH RE- CURRENCE	PER CENT. ALIVE, NO RECURRENCE	PER CENT ALIVE WITH RE- CURRENCE
1902 .....	24	19	15	4	0	21	—
1903 .....	26	21	12	9	0	43	0
1904 .....	32	24	14	10	0	41.7	0
1905 .....	51	43	23	18	2	41.8	46
1906 .....	57	51	34	17	0	33½	0
1907 .....	62	50	28	20	2	40	44
1908 .....	71	59	34	23	2	39	42.3
1909 .....	94	79	42	29	8	36.7	46.8
1910 .....	95	82	34	35	13	42.7	58.5
1911 .....	97	86	30	46	10	53.5	65

## CONCLUSIONS

1. Results in operations for cancer of the breast are as good as, if not better than, results in operations for cancer elsewhere.
2. The prognosis in younger people who received the benefit of an early operation was better than we had expected.
3. The prognosis is variable in a certain per cent. An extensive external involvement may give a fair prognosis, while a slight external lesion may terminate early from internal metastasis.
4. That metastasis may occur many years after the operation, though in the great majority of instances it will appear in the first few years, if at all. The difference between the percentage of patients living over three to five and ten years is not so great as might be expected, but this is because most patients who die of the disease die within the first three or at least the first five years. If they live five years, the probability of recurrence is small.

5. Comparing these results with those of former years would show that the results are improving, and that the improvement is due to the fact that patients are coming earlier for treatment rather than to any improvement or change in the technic of treatment.

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## THE HISTOGENESIS OF CANCER OF THE BREAST AND ITS CLINICAL SIGNIFI- CANCE\*

WILLIAM CARPENTER MACCARTY

The author desires that the subject of histogenesis be not confused with etiology. No direct reference to etiology will be made, although conditions which are closely associated with histogenesis will be described in order to give clinicians some knowledge upon which to base empirical therapeutics in view of no definite or absolute knowledge of any specific treatment for mammary carcinoma.

The subject as dealt with in this study has double significance. It is presented as additional knowledge to the general pathology of carcinoma, *i. e.*, to the apparent evolution of perverted, migratory and destructive epithelial cells (carcinoma) from cells which, under normal conditions, run a definite and rigid life-course in a cellular communistic life of well-being.

The second feature will assist teachers and clinicians in understanding more clearly the logical sequence of at least a part if not all the parenchyma of the epithelial neoplasms, which plays such a large rôle in the science of medicine.

This investigation was stimulated by the lack of applicability of published descriptions of histogenesis and the existing terminology of carcinoma of the mammary gland to the vast material, which has demanded clinical significance from the writer.

\* An abstract of this paper was read before the Southern Surgical and Gynecological Association, December, 1910, and published in the Transactions of the Association (vol. xxiii). Reprinted from Surg., Gyn. and Obst., October, 1913. 441-459.



Clinicians demand from the scientific world facts and utilitarian deductions. Their main object is the eradication or amelioration of physical suffering, and their patience is often taxed to the extreme by the overwhelming onslaughts of neoplasms, which only the courageous have seen fit to constantly empirically treat, first this way and then that, in hope of ultimate victory. The progress of the surgeon's efforts has been greatly impeded by a rich but chaotic terminology, for which he is partly responsible on account of insufficient knowledge of normal and pathologic processes and conditions. The pathologist, however, has shared in the production of this chaos by his withdrawal from the immediate field of the clinical activities of his practical colleague.

The clinician deals with specific and individual needs while the general pathologist has by or on account of his withdrawal found his problems general or purely biologic.

There are twelve apparent synonyms for the condition which Koenig described as "*mastitis chronica cystica*." They are found in American, English, German, French, and Italian literature and are doubtless to be found in the literature of other countries which have derived scientific inspiration and information from those already named. Unfortunately for the readers, especially the practitioner, all twelve synonyms do not appear in the same article. One writer utilizes one term and another utilizes another. Discussion, strife, misunderstanding, and discouragement have followed acceptance of various terminologies without a complete knowledge of the complete list of synonyms.

This extravagance of synonyms is but one example of the chaotic condition of terminology of pathologic mammary conditions. It is unharmonious, almost always undescriptive, semi-clinical, semi-scientific, often local in application, and frequently requires some knowledge of the life and works of some investigator for explanation.

Terms which embrace the names of abnormal processes, the physiologic processes of which are extremely indefinite, are utilized—"abnormal involution" (Warren) and "senile parenchymatous hypertrophy" (Bloodgood).

In the presence of such an indefinite condition of our knowledge one finds text-books and journals which continue to publish classifications of mammary tumors, especially carcinomas, which are dissimilar and are based on so-called definite entities. Thus many practitioners believe that "scirrhous carcinoma" and "medullary carcinoma" are two different things and indeed attribute very definite prognostic differences to each. When one adds to these terms the so-called "*comed-carcinoma*," "*adenocarcinoma*," "*encephaloid carcinoma*," "*carcinoma simplex*," "*cyst-adenocarcinoma*," "*carcinoma gelatinosum*," and "*carcinoma sarcomatodes*," the practitioner, who usually is not and cannot be conversant with all medical and scientific literature, necessarily either gives up trying to classify and name his own material or loses faith in the present presentation of the subject of pathology by pathologists. The lack of faith is well earned by the pathologist, who allows his profession to be maligned by the present utilization of interns, as pathologists, who innocently carry out the work of their partially trained teachers, who themselves have written or taught the above-mentioned and criticized chaotic terminology and classifications. As proof of the existence of terminologic extravagance one needs only to examine the following list, which is a compilation of the terms utilized in such excellent works as Adami and Nicholls' "Special Pathology," Kaufmann's "Spezielle pathologische Anatomie," 1911, Aschoff's *Spezieller Teil*, vol. xi, "Pathologische Anatomie," Borst's "Die Lehre von den Geschwülsten," Ziegler's "Lehrbuch der speziellen pathologischen Anatomie," E. Forgue's "Precis de Pathologie Extreme" (Collection Testut), The American Text-book of Pathology, and the text-book by Delafield and Prudden.

Mastitis: diffuse or interlobular  
 Acute galactophoritis  
 Chronic mastitis  
 Cirrhosis mammaræ  
 Mastitis carcinomatosa  
 Fibroma  
 Adenoma  
 Fibro-adenoma  
 Adenofibroma  
 Cystadenoma

Lipoma  
 Myxoma  
 Myoma  
 Angioma  
 Osteoma  
 Chondroma  
 Epithelioma  
 Carcinoma  
 Sarcoma  
 Adenosarcoma

Adenomyxoma	Sarcocarcinoma
Pericanalicular fibroma	Chondrosarcocarcinoma
Intracanalicular fibroma	Carcinoma chondrosarcomatosum
Intracystic papilloma	Carcinoma solidum
Fibroma cysticum	Carcinoma solidum simplex
Adenoma acinosum	Carcinoma solidum medullare
Adenoma tubulare	Carcinoma solidum scirrhusus
Scirrhous carcinoma	Carcinoma colloides
Medullary or encephaloid carcinoma	Carcinoma cysticum
Adenocarcinoma	Carcinoma cylindromatosum
Cystadenocarcinoma	Adenocarcinoma cylindromatosum
Simple parenchymatous mastitis	Cystocarcinoma papillare
Mastitis infectiosa parenchymatosa	Cystocarcinoma simplex
Mastitis infectiosa interstitialis	Cystocarcinoma papilliferum
Mastitis chronica cystica	Carcinosarcoma
Maladie cystique de la mamelle	Carcinochondrosarcoma
Cystadenoma polycystoma	Cancer en cuirasse
Intracanalicular cystadenoma	Acinal carcinoma
Mastitis tuberculosa obliterans	Fibro-adenoma pericanaliculare
Pure adenoma	Fibro-adenoma intracanalicular
Fibro-adenoma acinosum	Adenomyxofibroma
Fibro-adenoma tubulare	Adenolipofibroma
Fibro-pericanaliculare or plexiform fibroma or fibro-adenoma	Adenofibrosarcoma
Pericanalicular fibromyxoma	Cystadenosarcoma phyllodes
Fibromyxosarcoma	Solid adenoma
Fibro-adenoma cysticum	Cystadenoma papilliferum
Fibroma intracanalicular mammæ oedematosum	Blood cysts
Retention cysts	Milk cysts
Solitary cysts	Butter cysts
Galactocele	Involution cysts
Dermoid cysts	Psammocarcinoma
Epidermoid cysts	Colloid cancer
Cystosarcoma or cystosarcoma phyllodes	Melanoma of the nipple
Fibroma myxoma or sarcoma proliferum or arborescens	Perithelioma
Sarcoma papillare or polyposum	Hypertrophie vera mammæ
Cystadenoma papilliferum (i. e., intra- canalicular cystadenoma)	Mamma lactans
Cystic papillary epithelioma (fibro- epithelioma)	Fibro-adenoma mammæ
Fibromyxoma	Adenoma mammæ
Myofibroma	Fibro-adenoma mammæ peri- et intra- canaliculare
Hemangioma	Tubular adenoma
Enchondroma	Cystadenoma (phyllodes) mammæ
Osteochondroma	Cystadenoma (mammæ) pseudo-papilli- ferum
Round-cell sarcoma	Adenoma (mammæ) proliferans
Round and spindle-cell sarcoma	Carcinoma scirrhusus
Pure spindle-cell sarcoma	Carcinoma gelatinosum
Polymorphic cell sarcoma	Carcinoma adenomatosum
Giant-cell sarcoma	Carcinoma medullare
Angiosarcoma	Fibroma pericanaliculare
Melanosarcoma	Fibroma intracanalicular
Alveolar sarcoma	Adenoma mammæ acinosum
Chondrosarcoma	Adenocystoma
Endothelioma	Adenocystoma papilliferum
Osteoid sarcoma	Fibroma (sarcoma) phyllodes
	Adenomyxofibroma
	Adenosarcoma
	Cystoma mammæ papilliferum

Intracanalicular papillary fibroma or	Alveolar carcinoma
papillary adenocystoma	Cystic fibroma
Intracanalicular fibrosarcoma	Reclus' disease
Cystocarcinoma mammae papilliferum	Abnormal involution
Papillary cystocarcinoma	Senile parenchymatous hypertrophy
Acinar cancer	Solid fibroma
Tubular scirrhus cancer	Schimmelbusch's disease
Paget's disease	Cystic sarcoma
Tubular carcinoma	Solid sarcoma

In regard to our knowledge of carcinoma one finds two main groups of writers expressing themselves on its etiology, which is often confused with histogenesis. One group attributes the epithelial perversion to changes which take place primarily in the connective-tissue stroma of the breast. This primary change allows overgrowth and invasion by the epithelium. This theory has or has had many advocates, *i. e.*, Mintz, Ribbert, Lichtenhahn, Koenig, and others. The last-named investigator and perhaps others have departed from this belief.

Tietze, Saar, Schimmelbusch, Brissaud, Sicre, and Reclus have strongly advocated the primary change to be in the epithelium itself and not in the connective tissue.

There are still authorities who believe that the condition of carcinoma is the result of proliferation of both stroma and epithelium—Lichtenhahn, Koenig, Maly, Roloff, Stiles, and others.

The theory of "cut-off epithelium" or "epithelial embryonic rests" is very strongly fixed in the minds of the practitioner and older teachers as the origin of neoplasms.

Many authorities believe that carcinoma may develop on a "cystadenoma" or a "chronic mastitis." This belief has been expressed by Keibel, Tietze, Kuru, Bobbio, Fremicourt, Brehm, de Quervain, Verga, Sicre, Schimmelbusch, Reclus, Roloff, Franko, Sasse, and Koenig.

This suspicion remains, however, to be substantiated by fact. Nobody has ever seen such actual development take place. One may, however, scientifically state that carcinoma is seen in association with these conditions.

The "tumor process" or "neoplastic process" in the breast has been insinuated by Schimmelbusch, Sarr, Franko, Maly and others.

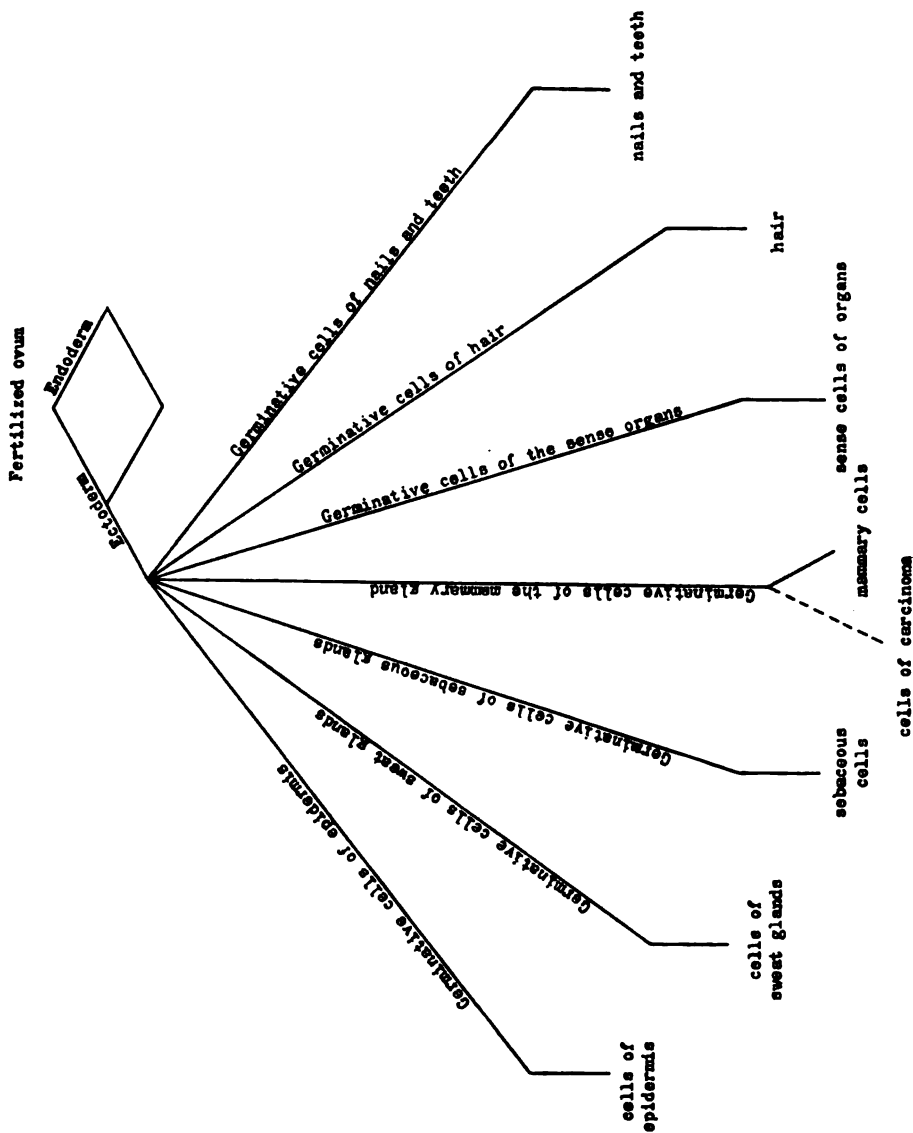


Fig. 162.—Diagram—Schematic representation of the relation of the ectoderm to the germinative cells of the skin and its appendages and the apparent biologic position of the cells which comprise carcinoma of the breast.

The interpolation of authors' names in this brief discussion of literature is made with the keen understanding that writers often change their opinions soon after the publication of their articles. They are mentioned here simply to emphasize the fact that the exact nature of the process is unknown. Writers, however, have continued to express themselves sufficiently emphatically to students to have stanch followers. Most of the views of the subject have been derived from a study of a limited material with limited impressions or perhaps to present a working hypothesis.

The limitation of the observed, described, published, and accepted material may be seen from the fact that each of eight out of eleven authorities who are frequently quoted drew and published conclusions from less than five cases.

Two authorities, whose names are attached to indefinite pathologic conditions\* in the breast, arrived at such eminence by describing a very small series of cases. Both articles were written, however, earlier than 1890—a fact which should make critics and future writers extremely charitable. Material was not so abundant and microscopic pathology was not so well developed at that period.

A large number (758) of cases was published by a surgeon (Warren). Pathologic reports were utilized instead of actual research on each specimen. Definitely diagnosed groups of apparent entities were utilized from which to analyze clinical and prognostic data.

With this brief critical summary of methods of investigation, record, and teaching of the pathologic conditions in the breast, one may proceed to a consideration of facts relative to the material at hand.

The material under consideration during this study in the Mayo Clinic consisted of 1000 amputated or excised human breasts for various pathologic conditions.

In this organ the so-called benign and malignant neoplasms and inflammatory conditions require removal and therefore supply a wide field for the investigation of epithelial cells under many

\* "Schimmelbusch's disease" and "Reclus' disease."

conditions. It supplies solid and cystic benign and malignant conditions. The epithelium is especially simple, beautiful, and definitely arranged under normal conditions.

The methods of investigation consisted of:

1. Studying the perfectly fresh specimens,\* both macroscopically and microscopically.

2. Repeated microscopic examinations of all portions of the organ by means of fixed sections stained with hematoxylin and eosin.

3. Large numbers of gross and microphotographs which, when studied collectively, give a comparatively complete picture of the neoplastic pathology of the organ. These pictures arranged themselves naturally according to similarity or identity and formed a series which begins with the simplest conditions of the units† (acini) of the organ and ends with the most extensive destruction of normal structure.

4. Repeated examinations of the material in order to confirm the natural photographic arrangement of the pathologic processes existing in and about the epithelium.

The embryologic or developmental facts, which are correlated with the writer's findings in this paper, are well known to embryologists and may be investigated by studying the works which are appended to this paper. If one traces the life-history of the mammary epithelium one begins with the ectoderm of the three-layer stage of embryologic development. This layer of partially differentiated epithelium becomes more highly developed to form the so-called skin of the embryo. At first it is composed of one layer of low cuboid cells, which, with further development of the embryo, becomes differentiated to form two or more layers of cells

\* All specimens were received into the surgical laboratory immediately upon removal. Frozen sections were made from many areas and stained with Unna's polychrome methylene-blue.

† The breast is composed of adipose tissue, connective tissue, and epithelial tissue. The last of these, or secreting portion of the breast, is arranged anatomically into gland groups which are composed of from 6 to 15 gland units. The gland unit or secreting unit represents the histologic unit of the organ and consists of several cells sharply demarcated from the stroma and arranged around a space or lumen which may be potential or patent.

(Figs. 163 and 164)—the outer layers differing from the first layer in being flatter or less cuboid with their long axes parallel with the surface of the body (Fig. 163).

With both antenatal and postnatal development the secondary layers become more differentiated and less like their immediate predecessors, which, in this stage, the embryologists have termed the "stratum germinativum"\* (Figs. 163 and 164)† of the skin or the germinating layer of the epidermis.

The history of the cells of this layer proves that they retain the power of divergence into several structural and functional derivatives. It may be spoken of as a plastic layer at least in the embryo. This expression of its broad functional capacity is based on its behavior in the development of the appendages of the skin; namely, hair, nails, sweat-glands, sebaceous glands, and the mammary gland.

Histologic specimens which have been taken through the embryonic skin and subcutaneous tissue in various portions show developmental activities of the stratum germinativum other than the production of epidermal cells.

\* Synonyms: Stratum germinativum, stratum cylindricum, basal epithelial layer.

† Illustrations and legends Figs. 163 to 172 are taken from Kiebel and Mall's Embryology.

Fig. 163.—Human fetus, 32 mm. in greatest length (collection of Prof. Robert Meyer, No. 307): Integument from the right side of the body; the epidermis is beginning to become three-layered: *P*, Periderm; *L*, stratum intermedium; *B*, stratum germinativum; *C*, corium, rich in cells; *G*, vessel (× 400).

Fig. 164.—Human fetus, 85 mm. vertex-breech length, male. Epidermis distinctly three-layered: *P*, Periderm with partly separated cells; *L*, stratum intermedium; *B*, basal layer of cells with mitosis; *C*, corium, rich in cells (mostly spindle-shaped). Mammary region (× 430).

Fig. 165.—Primary hair germ of human fetus, 8.5 cm. in length, male, from the mammary region. Two successive sections in which the circumscribed approximation of the nuclei is visible. The cells of the stratum intermedium have not yet increased in number and there is no increase of the connective-tissue cells of the corium (× 41).

Fig. 166.—Hair germ from the same region as Fig. 165. *H.-K.*, Hair germ; *L.*, increase of the cells of the stratum intermedium, and *C.*, of the connective-tissue cells of the corium; *Bl.*, periderm cell (× 430).

Fig. 167.—Longitudinal section of a hair germ of another 8.5 cm. human fetus, more advanced stage. *H.-Kan.*, hair canal cells (Stöhr). Spaces exist among cells of germ. *V*, anterior surface; *H*, posterior surface hair germ (× 430).

Fig. 168.—Transverse section of a hair germ in the same stage as Fig. 167 from pectoral region of the fetus of Figs. 165 and 166. Shows the distinctly symmetric structure and the kiln-like arrangement of the cells (× 430).

Fig. 169.—Hair-papilla from the upper lip of the fetus of Figs. 165, 166, and 168. *M.*, hair matrix with spaces at the converging point of the matrix cells; *Pa.*, anlage of papilla; *Hbg.*, connective-tissue hair sheath; *Bl.*, vesicular cells of the periderm; *V*, anterior surface of the follicle; *H*, its posterior surface with the (scarcely recognizable) differentiated arrangement of the nuclei (sebaceous gland and region of the hair swelling) (× 430).

Fig. 170.—Hair papilla in a more advanced stage, transition into the bulb papilla: *Pa.*, Anlage of papilla; *W*, swelling; *T.-Dr.*, anlage of sebaceous gland; *H.-Kan.*, hair canal cells; *H.-K.*, tangential section of a neighboring hair germ (× 430). (After Stöhr: Lehrbuch der Histologie, Fig. 300; Entwicklung des menschlichen Wollhaares, Fig. 9.)



Fig. 163.



Fig. 160.

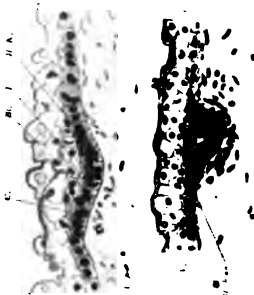


Fig. 170.

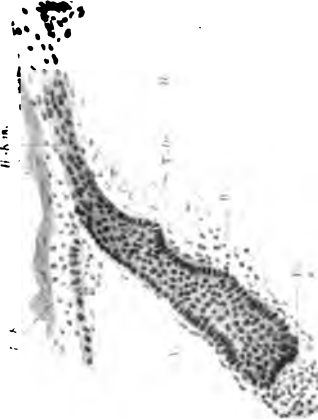


Fig. 164.



Fig. 168.

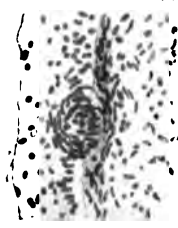


Fig. 165.



Fig. 169.

Fig. 171.—Sheath hair still near the bulb-papilla stage: *Pa.*, Papilla; *Gl.-H.*, vitreous layer; *W.*, swelling; *M. arr.*, musculus arrector pili; *H. Sch.*, inner root-sheath; *T.-Dr.*, sebaceous gland; *H.*, cells of the hair cone, not yet differentiated ( $\times 450$ ). (After Stöhr: Lehrbuch der Histologie, Fig. 302; Entwicklung des menschlichen Wollhaares, Fig. 14.)

Fig. 172.—A completely formed lanugo hair, from the mammary region of an eight-months' male fetus. Partly schematic, reconstructed with the camera lucida from an oblique series of sections: *P.p.*, cushion of connective-tissue papilla; *P.S.*, neck of papilla; *P.S.*, tip of papilla; *M.*, hair matrix; *Gl.-H.*, vitreous layer, for the most part separated from the outer root-sheath; *H.*, shaft of hair; *H. Sch.*, outer root-sheath; *Hbg.*, connective-tissue portion of follicle; *S.D.*, sudoriparous gland; *W.*, swelling; *T.-Dr.*, sebaceous gland; *H.-Ka.*, hair canal ( $\times 140$ ).

Fig. 171.

Fig. 172.

Figs. 166 to 177 inclusive show evidence of activity directed toward the development of hair-follicles. The downward growth of the cells of the "stratum germinativum" into the subcutaneous tissue is accompanied by their differentiation into hair instead of epidermis. The examination of a fully developed hair-follicle shows that there still remains a row of cells (Figs. 170 to 172 inclusive) which correspond to the "stratum germinativum" of the epidermis and may be considered the stratum germinativum of the hair. The epithelium of nails, sebaceous glands (Fig. 178), sweat-glands (Figs. 173 to 177 inclusive), and mammary glands (Figs. 179, 180, 181) possesses its stratum germinativum, from which its differentiated cells are reformed.

From this brief statement of embryologic facts and the photographic facts which are presented here one may crudely construct a working diagram of the probable histogenetic position of the cells which form carcinoma.

Figs.\* 182 (A27943),† 183 (A8743), and 184 (A27943) were taken from sections of adenofibroma and non-carcinomatous portions of carcinomatous breasts. The acini vary greatly in size, some are atrophic, some cystic, and some hypertrophic. They are separated by a fairly dense, irregular interacinar stroma. A few lymphocytes are seen in the field. These pictures correspond to many of the pictures which are published in the literature as "abnormal involution," "senile parenchymatous hypertrophy," "Schimmelbusch's disease," "maladie de Reclus," and "mastitis chronica cystica." Such pictures are almost always present in chronic cystic mastitis.

In Figs. 185 (38463), 186 (A27943), 187 (26079), and 188

\*Pathologic diagnoses of cases utilized to illustrate this paper:

A27943 ... Fibro-adenoma	31329 ... Carcinoma
A8743 ... Fibro-adenoma	30694 ... Carcinoma
26079 ... Extensive carcinoma	A41253 ... Carcinoma
36138 ... Carcinoma	26166 ... Carcinoma
28376 ... Carcinoma	50132 ... Carcinoma
36116 ... Carcinoma	38463 ... Carcinoma
A12998 ... Chronic mastitis	20797 ... Fibro-adenoma
35256 ... Carcinoma	A74345 ... Carcinoma
22595 ... Carcinoma	29785 ... Carcinoma

† Numbers in parentheses preceded by A are office numbers. Those without the A are hospital numbers.

Fig. 173.



Fig. 174.

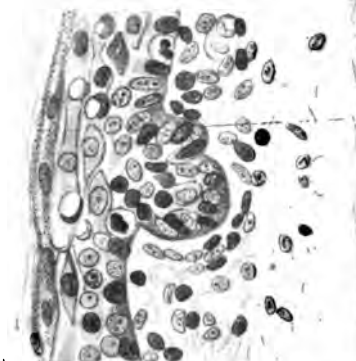


Fig. 175.

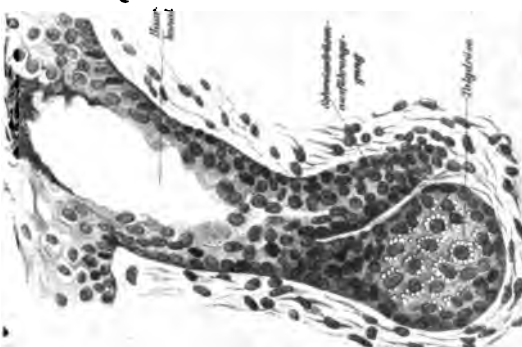
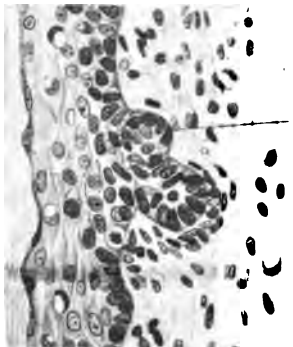


Fig. 176.

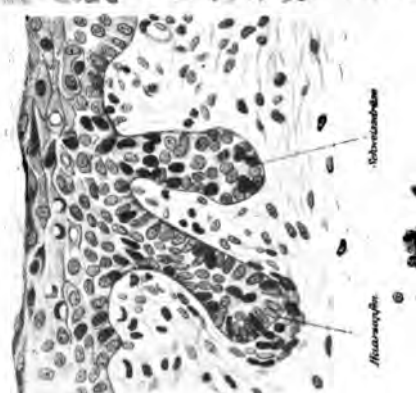


Fig. 177.

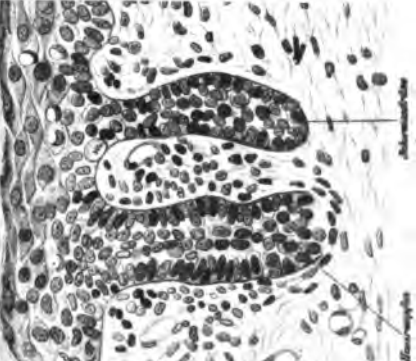


Fig. 178.

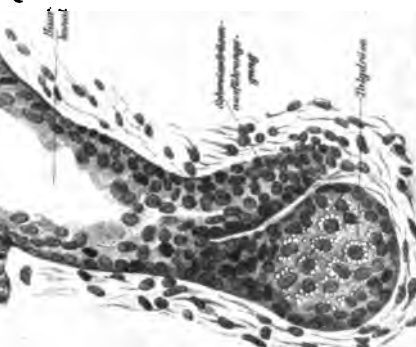


Fig. 173.—The formation of the "anlagen" of a hair-follicle and sweat-gland from the stratum germinativum. (Taken from Fig. 38, C. Wimpfheimer, Anat. Hefte, I. Abtheilung, 104.)

Figs. 174-177.—Showing the further development of the "anlagen" of the hair-follicle and a sweat-gland (Fig. 173) (C. Wimpfheimer).

Fig. 178.—Showing the relation of the "anlage" of sebaceous glands to the epithelium of the skin (C. Wimpfheimer).

(26079) one sees higher magnifications of acini similar to those

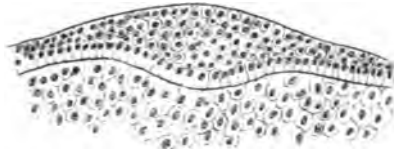


Fig. 179

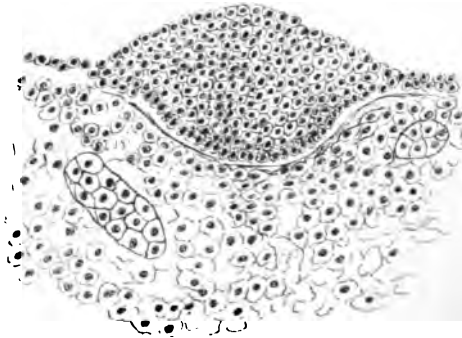


Fig. 180.

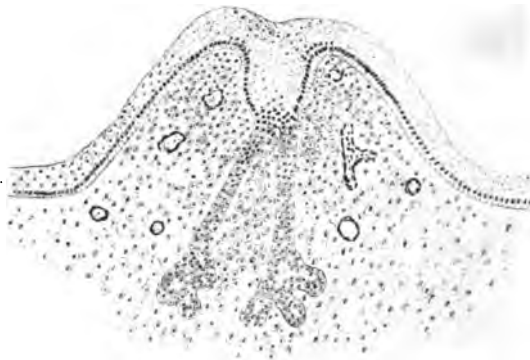


Fig. 181.

Figs. 179, 180, and 181.—Presenting the development of the mammary gland from the stratum germinativum of the skin. (Copied from illustrations in the "Lehrbuch der Entwicklungsgeschichten von Dr. Robert Bonnet.")

which are seen in Figs. 182, 183, and 184. In all, each acinus is composed of two rows of epithelial cells, the two rows being more

Fig. 184.

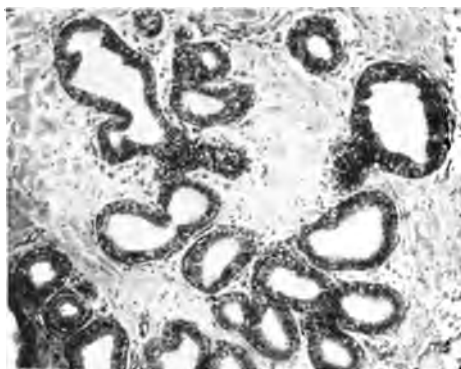


Fig. 183.

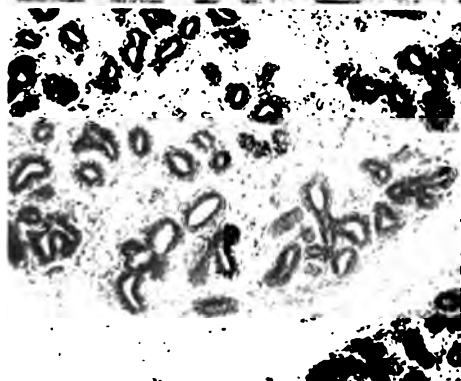


Fig. 182.

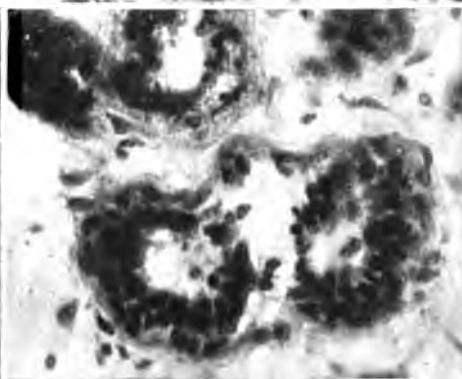
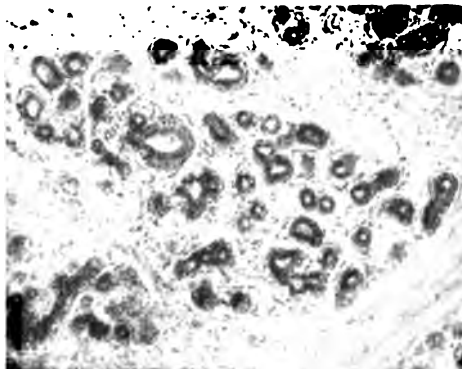
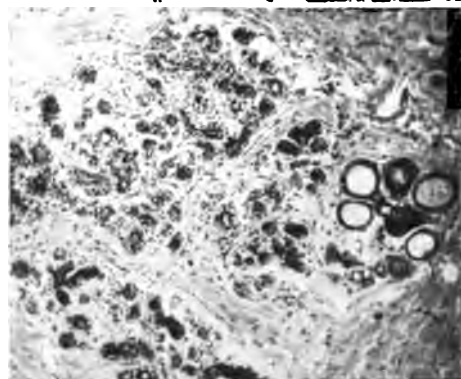


Fig. 187.

Fig. 186.

Fig. 185.

Figs. 182 (A27945), 183 (8743), 184 (A27945), 185 (88463), 186 (A27943), 187 (26079).—Sections taken from adenofibromas and non-carcinomatous portions of the mammary gland. The pictures are similar to some of those which have been published under the heading of "abnormal involution" (Warren), and described by Koenig as "mastitis chronica cystica." Epithelium in the stage of *primary hyperplasia*.

prominent in Figs. 188 and 189. The cells are evidently hypertrophic and hyperplastic. Those lying next to the lumen are more deeply stained, have dense protoplasm and oval nuclei. They are apparently more highly differentiated than those of the outer row, and are the secreting cells of the acinus. The cells of the outer row have clear, rare protoplasm; the nuclei are round; the cells are less differentiated; they are more embryonic. They form the "stratum germinativum" for the secreting cells of the acini.

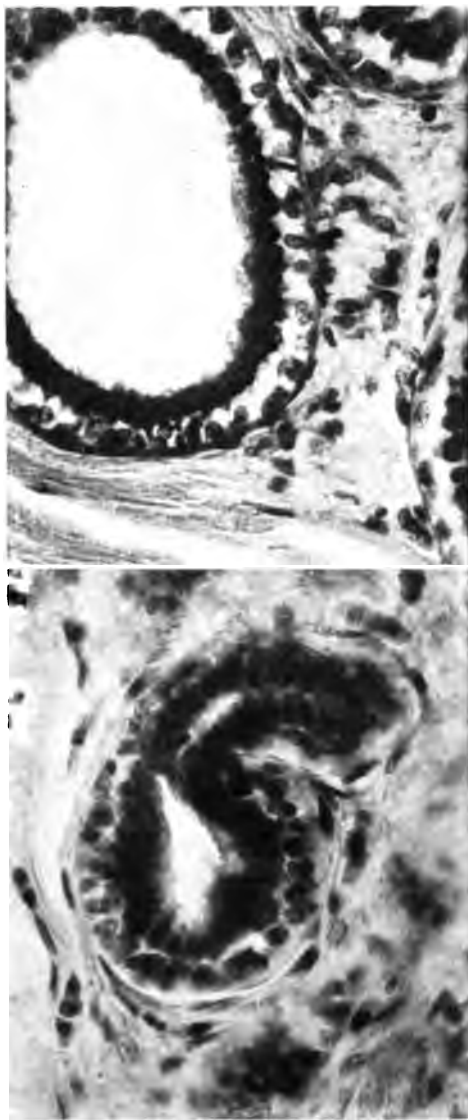
In Fig. 190 (36138) the inner row of differentiated cells has completely disappeared, leaving only the less differentiated cells of the outer row. The acini are surrounded by active, proliferating connective-tissue cells.

In Fig. 191 (28376) the cells of the outer row or the undifferentiated cells are hyperplastic and have filled the entire lumen. None of the cells of the inner row are to be seen.

In Fig. 192 (36116) the acinus is formed by hyperplastic cells of the outer row. They are large and irregular in shape and size. In the center of the acinus the detritus of disintegrated cells is seen. The periacinar connective tissue is composed of active fibroblasts.

The acini in Fig. 193 (12998) are filled with disintegrating hyperplastic cells of the outer row. This picture corresponds to some of those published in the literature as "Schimmelbusch's disease," "senile parenchymatous hypertrophy," "maladie de Reclus," and "mastitis chronica cystica." It will be noted that the periacinar connective tissue is dense. It is not filled with lymphocytes or proliferating fibroblasts. This association of dense connective tissue with complete necrosis of the cells of the acinus may be seen also more distinctly in Figs. 226 to 229, in which there is formed a definite barrier of connective tissue surrounding the acinus.

Figs. 194 (36116) and 195 (36116) present acini which are composed of only one row of cells which correspond to the cells of the outer row of undifferentiated cells. They are hypertrophic, hyperplastic, and exceed the normal limits of size and shape of the cells of the outer row. In the center of the acinus one finds dis-



Figs. 188 (36079), 189 (36138).—Acini from a non-carcinomatous portion of a carcinomatous breast. The cells of the acini form two distinct rows (inner and outer rows). This condition is common in chronic cystic mastitis, "abnormal involution," "senile parenchymatous hypertrophy," "Schimmelbusch's disease," "maladie de Reclus," "cystadenoma and so-called benign fibro-epithelial neoplasms. Under the heading of hyperplasia it is considered *primary hyperplasia*.

integrated material, which, when studied in relation to the foregoing pictures, is probably disintegrated epithelium.

Fig. 196 (36116) shows a similar acinus with a break in the acinar wall.

Fig. 197 (35256), which is a lower power photograph, shows a number of acini which answer the descriptions given for Figs. 188, 189, 190, 191, and 192, and show clearly the great distortion of the acinar outlines, with confusion of cells between the stroma and the epithelium.

Fig. 198 (36116) presents a picture of hyperplastic epithelium frequently seen in "chronic cystic mastitis," and practically always in association with definite invasion of tissue.

Figs. 199 (31329), 200 (31329), 201 (31329), 202 (30694), and 203 (22595) show the morphologic similarity of the extra-acinar cells (carcinoma cells) to the intra-acinar cells which have been seen in the acini in the preceding pictures. They are definitely carcinoma, and present the cellular characteristics which are present in cells which have not "broken through" the so-called "basement membrane"—the accepted morphologic criterion of malignancy.

Figs. 204 (A41253), 205 (A41253), 206 (26166), and 207 (26166) show extensive invasion of tissue by perverted epithelium.

The morphologic characteristics of the epithelium which lines mammary cysts is similar to that which has just been described.

Fig. 208 (A27943) is a section through a specimen of chronic cystic mastitis showing small cystic acini.

Fig. 209 (50132) is a photograph of fresh tissue showing inter-acinar bridges in one stage of the process of destruction.

In Fig. 210 (35256) the acini of a gland group may be seen in the process of fusion to form cystic areas.

Figs. 211 (12998) and 212 (29785) show acini which have become united and form pseudopapillæ which have been covered over with epithelium, which is arranged in two definite layers comparable to the arrangement which is seen in the acini in Figs. 188 and 189.

In Figs. 213 (38463) and 214 (38463) a distended cyst is seen. It is lined by the same two layers of epithelium which are found in Fig. 188.



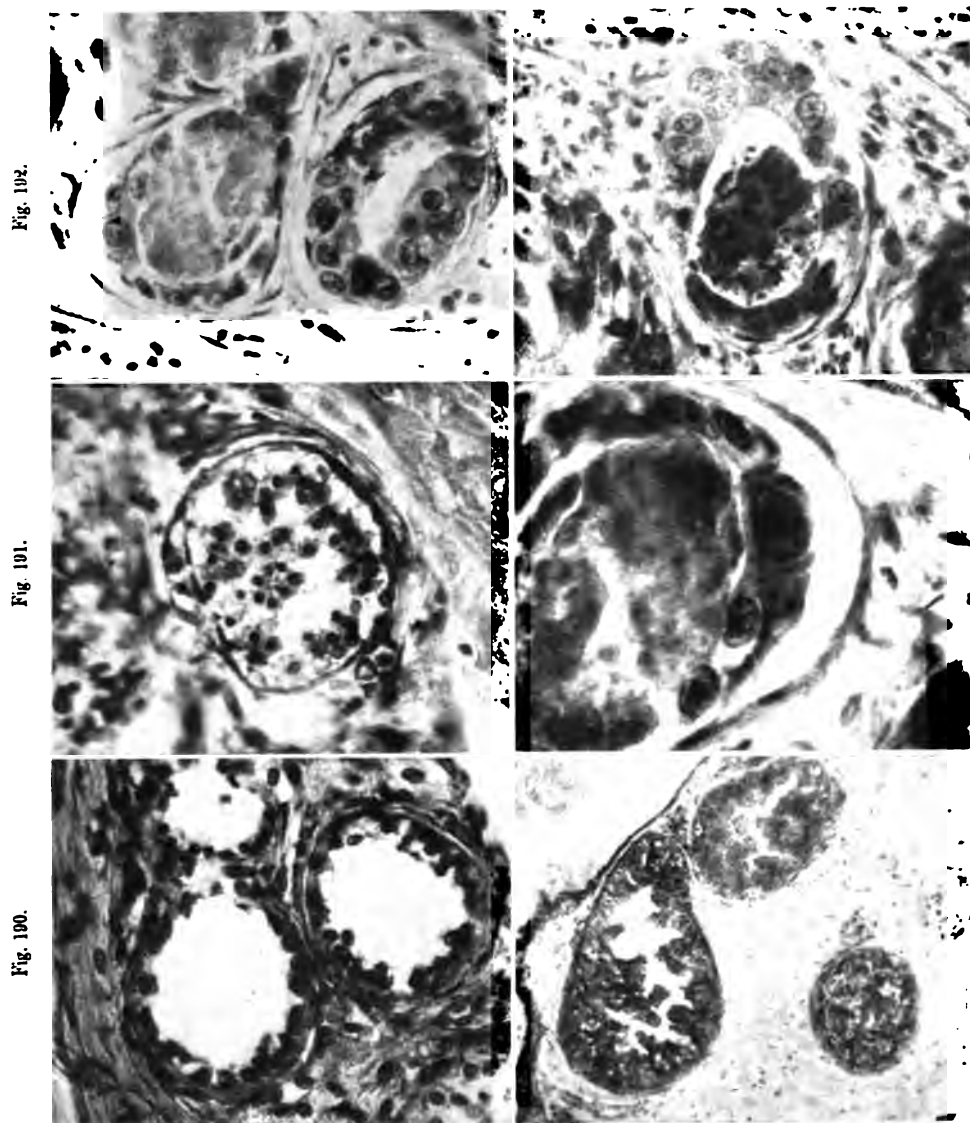


Fig. 102.

Fig. 101.

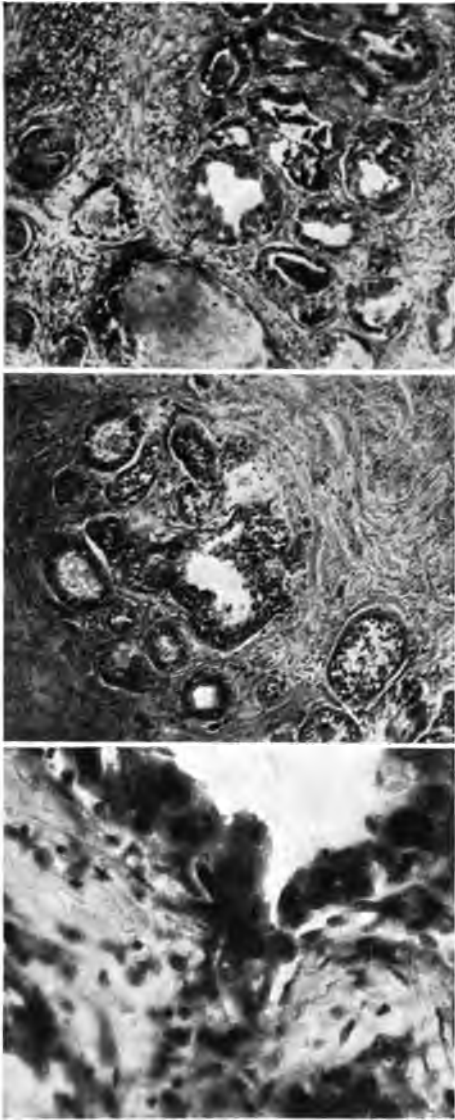
Fig. 100.

Fig. 195.

Fig. 194.

Fig. 193.

Figs. 190 (36138), 191 (36376), 192 (36116), 193 (19298), 194 (36116), 195 (36116).—Secondary hyperplasia in sections from chronic mastitis and carcinomatous breasts. The inner row of cells has disappeared and the outer row has become hyperplastic. The cells are indistinguishable from the carcinomatous cells in Figs. 196, 200, 201, 202, and 203.



Figs. 196 (36116), 197 (35256), 198 (36116).—*Tertiary hyperplasia*. The cells are apparently similar to those in "secondary hyperplasia." The line of demarcation between the parenchyma and the stroma is indefinite or partially destroyed.

Fig. 199.

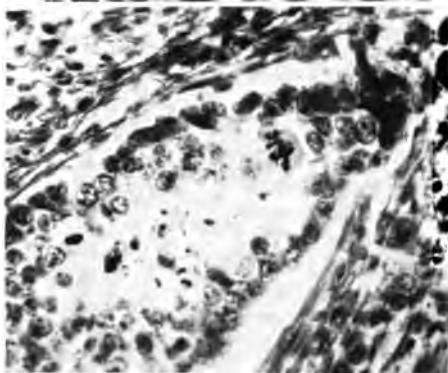


Fig. 200.

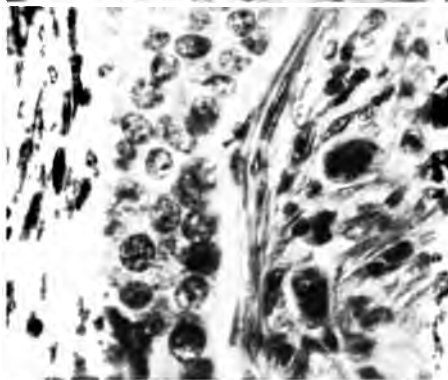


Fig. 201.

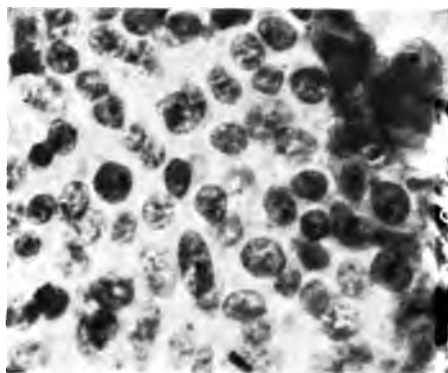


Fig. 202.

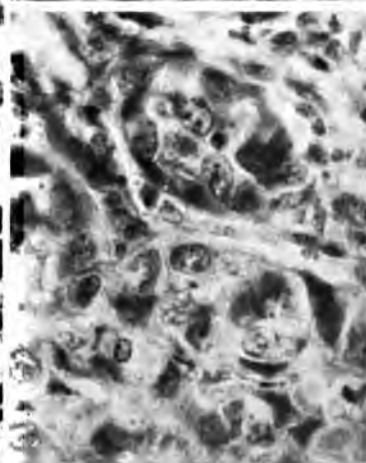
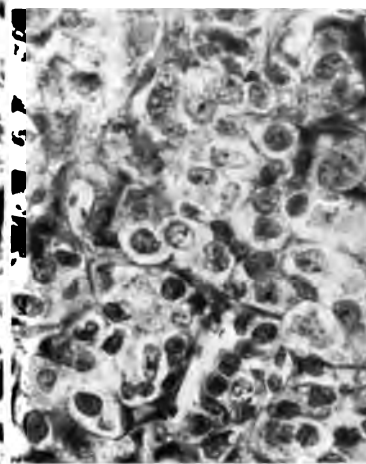


Fig. 203.



Figs. 199 (31329), 200 (31329), 201 (31329), 202 (30694), 203 (32595).—*Tertiary hyperplasia* (migratory hyperplasia) showing morphologic characteristics of the cells of carcinoma in the stroma of the breast.

In Figs. 215 (12998) and 216 (12998) one finds distended acini which are a part of a gland group composed of 7 acini. Unlike the cyst which has been seen in Fig. 213, there is only one layer of epithelium lining most of the wall. There is, however, an extensive hyperplasia of the cells similar to that seen in Figs. 190 to 198 inclusive.

In Fig. 214 (38463) may be seen the character of the cells which arrange themselves in two rows to line simple cysts. This picture may be compared to Figs. 217 (36116), 218 (20797), and 219 (36116), in which the inner row of cells has completely disappeared and is replaced by hyperplastic cells of the outer row. The nuclei of the cells are irregular in size and shape beyond the normal limits of size and shape. Many of the cells are apparently necrotic. The line of demarcation between the epithelium lining the cyst and the periacinar stroma is sharp. A few lymphocytes are seen in the stroma.

In Figs. 218 (20797) and 216 (12998) one finds hyperplastic cells lining the cyst. The nuclei are irregular in shape and size. The line of demarcation is less sharply defined. In Fig. 219 (36116) the line of demarcation is still less defined, the epithelial cells are hyperplastic and very irregular in shape and size.

Fig. 220 (A74345) with its accompanying small pictures (221, 222, 223, 224, and 225) is important in showing the variety of epithelial cells which may be present in the same field of the microscope. Two cysts are present: one is lined by several layers of small oval and round epithelial cells. The second cyst is lined by low cuboid cells and columnar cells. Near the cysts we see acini filled with large cells with small, round nuclei. These cells are indistinguishable from the cells which one finds characteristic of sebaceous glands.

The last picture is frequently found in the breast, and doubtless has been responsible for the speculation of a few observers who have written about the possibility of carcinoma of the breast arising as a result of misplaced sebaceous glandular elements.

The photographs herewith presented represent a composite picture of pathologic conditions in the breast other than sarcoma,

Fig. 303.

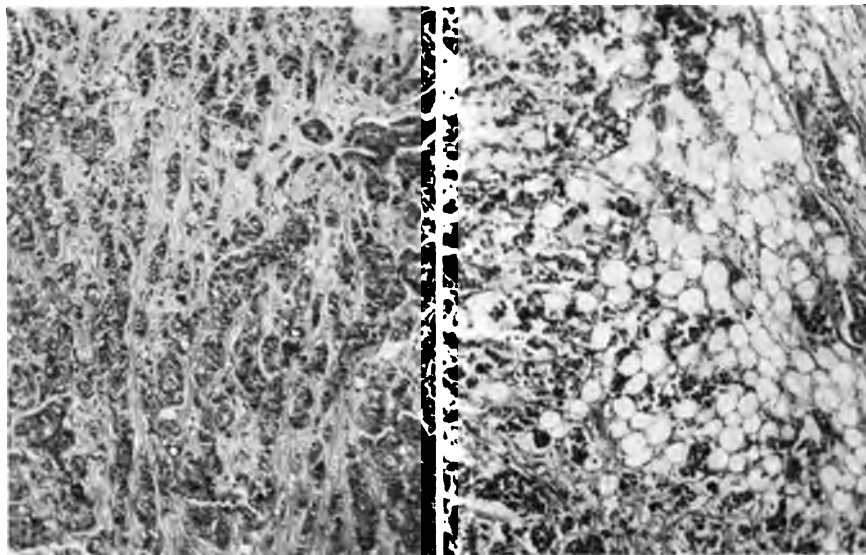


Fig. 307.

Fig. 304 (A41253), 305 (A41253), 306 (26166), 307 (26166).—Tertiary hyperplasia (migratory hyperplasia) showing low-power morphology of the stroma which is invaded by carcinomatous cells.

Fig. 304.

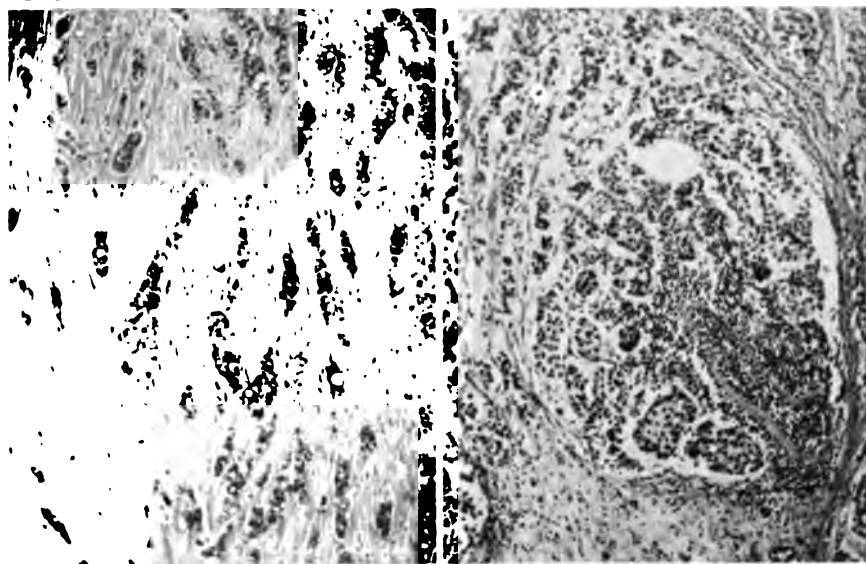


Fig. 306.

chondroma, tuberculosis, myxomas, and such rarer conditions as actinomycosis and abscesses, and are clearly those found in chronic cystic mastitis and carcinoma. Similar epithelial hyperplastic conditions are also seen in encapsulated tumors, such as adenofibromas, fibro-adenomas, and intracanalicular fibromas.

The usual behavior of the epithelium of the acini under conditions of chronic inflammation—without any reference whatsoever to the cause of the condition—is herewith seen photographically.

The breast, as seen in operative material, frequently shows evidence of chronic inflammation, which is indicated by varied amounts of lymphocytic infiltration, connective-tissue and epithelial proliferation, acinar distortion, epithelial necrosis, exfoliation, and hyaline degeneration.

The pictures which have been described and published in the literature under the titles of "chronic cystic mastitis," "abnormal involution," "senile parenchymatous hypertrophy," and "Schimmelbusch's disease" are similar to the pictures which are presented in Figs. 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 209, 210, 211, 213, 214, 215, 216, 217, and 218.

Where to draw the line between the hyperplastic changes of chronic cystic mastitis and the pictures which are definitely carcinoma is beyond the writer's present power. A careful study of the illustrations shows that there is no apparent sharp line of demarcation. One condition merges into the other.

Why all cases of chronic cystic mastitis are not associated with carcinoma is no more answerable than why the acute bacterial diseases do not terminate fatally in all cases and why all cases do not carry out their course in exactly the same manner and with the same amount of destruction. Bodily resistance, whatever that means, doubtless plays a rôle in the progress of epithelial neoplasia, just as in the case of any other pathologic conditions.

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Figs. 208 (A77943), 209 (50123), 210 (35256), 211 (12993), 212 (29785), 213 (38463), 214 (38463) show the evolution of at least some of the cysts which occur in the mammary gland. The stages are apparently dilatation of acini, fusion of acini, formation of pseudopapillae, further distention with disappearance of the pseudopapillae. The epithelium is in the two-layered stage of hyperplasia (primary hyperplasia).

Fig. 208.

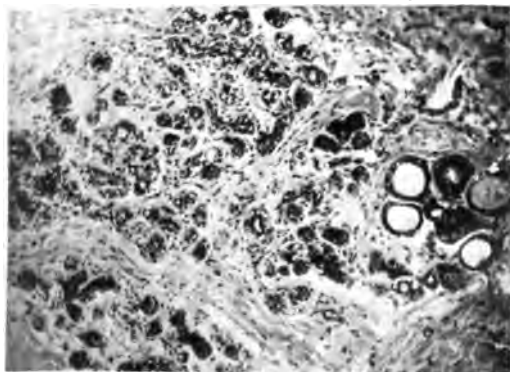


Fig. 209.

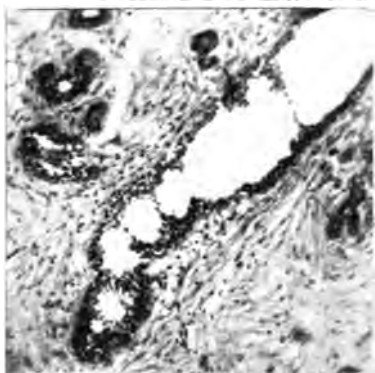


Fig. 210.

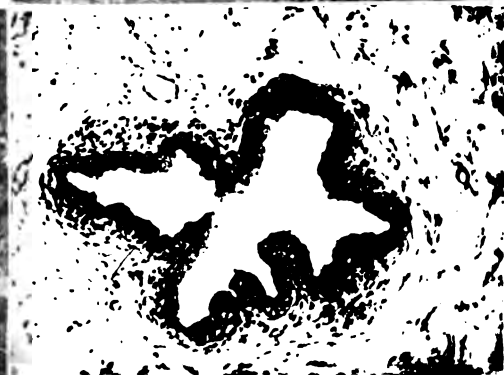


Fig. 211.

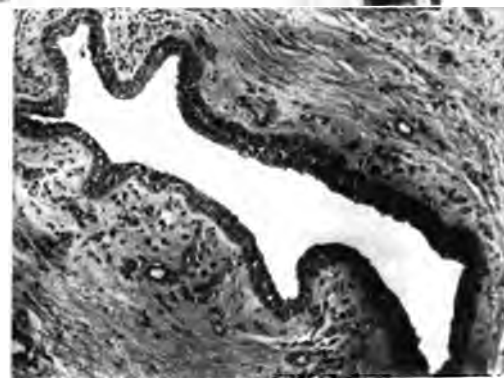


Fig. 212.  
Figs. 208-213.

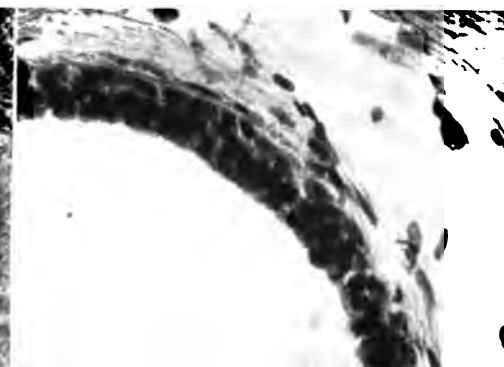


Fig. 213.



Fig. 214.

The part played by the stroma in epithelial hyperplasia and neoplasms varies considerably, as is seen in Figs. 226 (36116), 227 (29785), 228 (36116), and 229 (36138).

The question of why and how this defensive warfare is carried on in the body is one of the fields of pathology and physiology which have been barely touched by the scientific world.

So far as the histogenesis of carcinoma is concerned in the breast, one may say that not infrequently, usually between lactations or shortly after the menopause, certain changes of a chronic inflammatory nature occur, and that associated with these changes one finds a hyperplasia of the epithelium of the acini, characterized by prominence of the outer row of cells (stratum germinativum), and that frequently in one or more portions of the breast the inner row or secreting cells are exfoliated and not renewed by the outer row. Instead of renewal of functional or differentiated cells, the stratum germinativum continues to proliferate into the acinar lumen in an undifferentiated condition.

In this condition of the acini the interacinar septa often become thinner and disappear, thereby producing a cyst by coalescence. This coalescence occurs with and without the presence of the two layers of epithelium. In the presence of the hyperplasia of the outer row the line of demarcation between parenchyma and stroma frequently is confused and is often absent, with invasion of the periacinar stroma by the same cells, or at least cells indistinguishable from the cells of the outer row. This last condition produces the histologic picture which is recognized as carcinoma, which clinically is almost always if not always malignant.

An analysis of epithelial hyperplasia and neoplasia in the light of the development of epithelium of the breast may lead some investigator to determine more accurately the exact biologic position of the so-called carcinomatous cells which we know are contrary in action to the activities of normal cells under a communistic life.

In the terms of hyperplasia three grades may be recognized in the breast. These are the morphologic extremes of an apparent process of transition, the transitional stages of which supply no distinctive terminology.



Fig. 215.

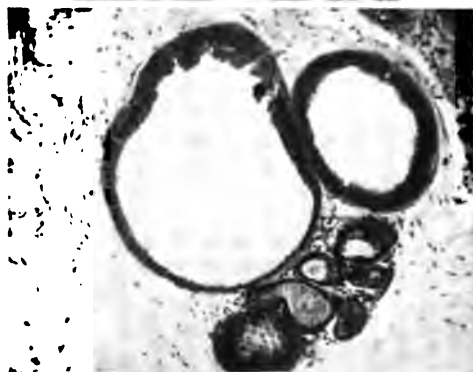


Fig. 216.



Fig. 217.

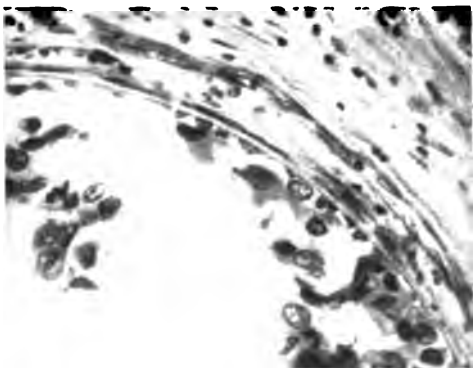


Fig. 218.

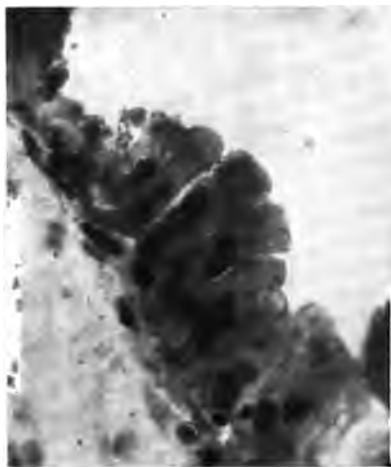
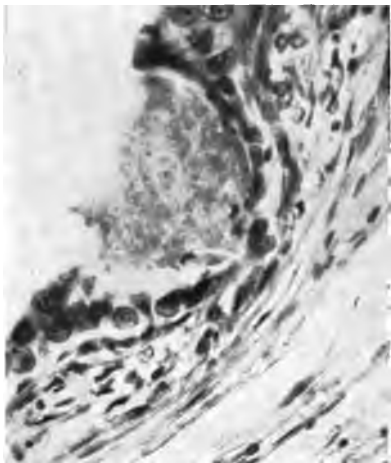


Fig. 219.



Figs. 215 (12998), 216 (12998), 217 (36116), 218 (20797), 219 (36116) show secondary hyperplasia of the epithelium of cysts in carcinomatous breasts. The inner row of epithelial cells has disappeared, the outer row is hyperplastic, and the cells themselves are indistinguishable from those which are seen in Figs. 190 to 203.

Under the head of *primary hyperplasia* one may group all of the hyperplastic epithelial morphologic evidences of activity which pertain to the combined activities of both the differentiated cells and the undifferentiated or germinal cells. All conditions in which both rows of cells exist and partake in the reactions may be spoken of as primary hyperplasia.

Under the head of *secondary hyperplasia* one sees only the activity of the germinative or undifferentiated cells within the confines of the acinar limits. They have failed to produce the differentiated cell.

A third grade—*tertiary hyperplasia*—is recognizable in the extra-acinar or migratory activities of the cells which apparently originated in the germinative cells (cells of the outer row\*).

The question which immediately rises on the presentation of such a simple conception of hyperplasia—of which carcinoma is here considered a part—is, What clinical and prognostic deductions may be drawn?

This question, with our present knowledge, cannot be momentarily answered any more than the clinician can accurately prognosticate according to the terminology of the so-called “types” of carcinoma which he utilizes at present. The favorite question of the clinician is, What kind of cell constitutes the neoplasm? In the writer’s experience only two apparent extremes even suggest prognostic difference, namely, the so-called “medullary or cellular carcinoma” and the “scirrhous carcinoma.” Intermediate gradations between these so-called entities exist, and often both “types” exist in the same tumor—indeed, in the same field of the microscope.

Again, in the summation of our real knowledge it seems that we are forced to admit, when not deceived by the suggestion of empiricism, that accurate knowledge of the activities, the duration of activities of epithelium, and the bodily defensive forces against malignant invasion, is still in the realm of research.

Such a statement of facts may seem pessimistic. On the contrary, however, they represent merely the “taking stock” of

\* Stratum germinativum of the mammary epithelium.

Fig. 220.

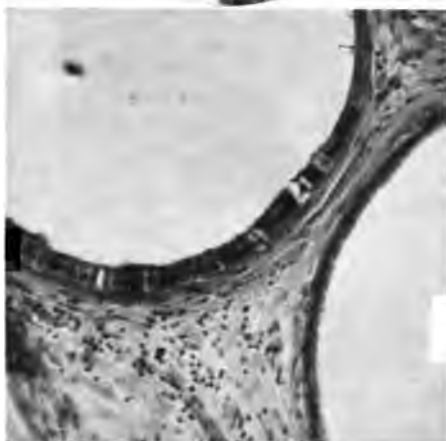


Fig. 221.



Fig. 222.

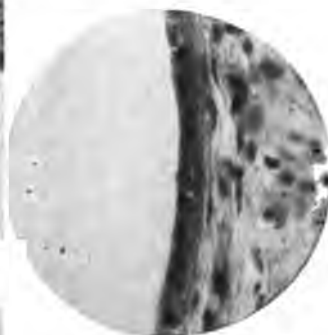


Fig. 224.

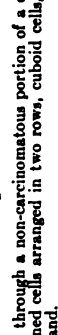


Fig. 225.

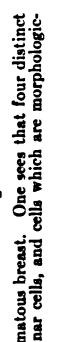


Fig. 223.

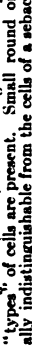


Fig. 220 (74545) shows a single microscopic field through a non-carcinomatous portion of a carcinomatous breast. One sees that four distinct "types" of cells are present. Small round or flattened cells arranged in two rows, cuboid cells, columnar cells, and cells which are morphologically indistinguishable from the cells of a sebaceous gland.

Figs. 221, 222, 223, 224, and 225. - Higher magnifications of the different types of epithelium in Fig. 220 (74545).

things as they are and not as we are prone to think they are in our partially empirical efforts to accomplish things.

So far as the epithelial activities in the breast are concerned with the therapeutic efforts of the clinician, the present conception offers him a greater chance of doing more good when his efforts are controlled by the activities of those specially trained in the recognition of the stages herewith presented.

It immediately gives him a logical grouping for his material, a grouping which is based on definite morphologic and easily recognizable conditions. It presents three distinct conditions, which can be studied in conjunction with good preoperative and post-operative histories. The morphologic entities are not based on such an indefinite histologic structure as the "*membrana propria*," which is only occasionally demonstrable, even under normal conditions.

On a careful study of the pictures presented here, which represent the findings in a large series of cases, the following deductions may—it seems to the writer—be made:

It may readily be seen that there is a definite pathologic foundation for the surgical experience that the conditions described as "senile parenchymatous hypertrophy," "abnormal involution," "cystadenoma," and "chronic cystic mastitis" are often, if not always, associated with carcinoma.

In a single specimen may be seen the stages through which this association probably takes place.

One also finds histologic pictures in specimens of carcinoma which correspond to those described by many writers as "cystadenoma," "papillary cystadenoma," "intracystic epithelioma," "Schimmelbusch's disease," "chronic interstitial mastitis," "chronic cirrhotic mastitis," "chronic cystic mastitis," and "polycystic epithelial mastitis."

Carcinoma is apparently an outgrowth of the outer row of cells of the acini and not of the secreting cells, and also is not the product of "cut-off" epithelial cells by scar tissue, but is derived from the stratum germinativum.

The cells of the outer row of the acini form the growth into the

lumen described by Schimmelbusch as cystadenoma. The proliferating cells of the acini—whether these acini are cystic or not after the disappearance of the inner row of cells—present the same irregularities of the nuclei which are seen in the cells which have invaded the stroma, lymph-spaces, and lymph-nodes. They are irregular in size and shape beyond the normal limits of size and shape of the normal cell. This irregularity is present in the acini, the so-called “basement membrane” of which is still intact.

The practical question, therefore, arises: Is it necessary to wait for the penetration of the “basement membrane” before making a diagnosis of carcinoma? From the standpoint of the general pathologist this may be necessary, but if the surgeon waits for such a change he will be basing his procedure upon a definition of carcinoma which does not consider the same characteristic in the cells before and after the penetration of the “basement membrane” distinctive of carcinoma. If the pathologist considers the penetration of the “basement membrane” the essential characteristic of carcinoma, then it must be admitted that the cells in chronic mastitis and cystadenoma are often just as irregular as in carcinoma and are indistinguishable from those of carcinoma.



Figs. 226 (36116), 227 (29785), 228 (36116), and 229 (36138) show the periacinar reaction which often occurs in association with carcinoma.

A more careful and detailed study of carcinoma cells, "cyst-adenoma" cells, the hyperplastic epithelial cells of fibro-adenoma and of chronic cystic mastitis has demonstrated that the resemblance between these cells is so great that if the desired therapeutic effect is to be accomplished, more "benign" tumors (fibro-adenoma, adenofibroma, and cystadenoma) must be completely enucleated and more breasts diagnosed as "chronic cystic mastitis," "abnormal involution," or "senile parenchymatous hypertrophy" must be completely removed.

On account of the close morphologic relation between these conditions the diagnosis must be made and the therapeutic measures carried out early in order to save the patient from the ravages of the extensive hyperplastic migratory epithelial conditions which we call carcinoma.

Gross diagnosis, even when made by an expert, can be made in only a certain percentage of cases. The early change is microscopic, especially in fibro-adenomas and chronic cystic mastitis.

Early diagnosis must be carried out regardless of the age of the patient, because carcinoma occurs in a wide range of ages. The youngest of this series was aged twenty-three years, the eldest, seventy-two years, and the average age was forty-seven years. The youngest "benign" fibro-epithelial tumor occurred at nineteen years, the eldest at sixty-five, and the average thirty-three years.

The surgeon as well as the pathologist should look upon the histogenesis of carcinoma as a process which apparently bears a most striking relationship to circumscribed and diffuse cystic or non-cystic fibro-epithelial hypertrophies and hyperplasias of the breast.

With our present knowledge of conditions of the mammary epithelium it behooves the pathologist and the clinician to accept a simple biologic conception of epithelial activities in the terms of primary, secondary and tertiary hyperplasia, rather than to attempt a scientific grouping of cases according to an unscientific and chaotic nomenclature.

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CLINICAL SUGGESTIONS BASED ON A STUDY  
OF PRIMARY, SECONDARY (CARCINOMA),  
AND TERTIARY OR MIGRATORY (CARCI-  
NOMA) EPITHELIAL HYPERPLASIA OF THE  
BREAST \*

WM. CARPENTER MACCARTY

The writer's reasons for making the following contribution to the pathology and therapeutics of the breast may be briefly stated.

An examination of the literature reveals that there are at least 147 different terms which are utilized to express pathologic mammary conditions. These are confusing to the great majority of practitioners, surgeons, teachers, and students.

Many of these terms are synonyms, an example of which may be seen in the fact that there are 12 synonyms for the condition which Billroth and Koenig described as "mastitis cystica chronica."

The classifications which have been and are utilized are numerous and very different. This may be seen also in the fact that the best authorities disagree upon the character of such conditions as "cystadenoma," "abnormal involution," and "senile parenchymatous hypertrophy." These may be found described by some writers as benign conditions, and by others as malignant conditions.

The clinical uncertainty which exists as a result of the confusion of terminology, the multiplicity of classifications, the divergence of operative advice from the general pathologist, and the lack of recognition of carcinoma as a part of an epithelial hyperplasia has occasionally led to radical amputations of breasts unnecessarily and also has allowed tumors which were clinically benign to remain in the presence of a possibility of malignancy.

\* Read before the Southern Surg. and Gyn. Assoc., Atlanta, December 16-18, 1913. Reprinted from Surg., Gyn. and Obst., 1914, xviii.

The fact that general pathologists have recognized only epithelial hyperplasia into the stroma as carcinoma has led to advice to the surgeon which has often proved to be disastrous.

The dogmatism relative to the rôle which the very indefinite "basement membrane" has played in being the histologic arbitrary line of demarcation between benign conditions and malignant conditions has often retarded surgical radicalism, which is, with our present knowledge, absolutely necessary in the treatment of cancer.

These existing conditions have stimulated a series of investigations of the pathology of 1000 breasts. It has been thereby shown that there are three definite histologic pictures which form a logical basis upon which operative procedure may be carried out.

The mammary acinus (gland unit) (Figs. 230, 231, and 232) is composed of one row of columnar or cuboid epithelial cells, which are the functioning or secretory cells.

These rest upon another layer of cells, which are almost invisible in the normal breast, but which become prominent when there is a chronic inflammatory reactive process present (Fig. 232). These correspond to the so-called "stratum germinativum"\* of the skin, and are the cells which are the progenitors of the differentiated or secretory cells. They constitute the germinal cells of the epithelium of the breast. In the presence of chronic inflammatory reaction in the mammary gland one or more of three histologic pictures (Figs. 231, 232, 233, 234, 235) are seen, regardless of whether the condition be encapsulated or non-encapsulated.

When the differentiated cells (inner row) and the undifferentiated cells (outer row) are present, the histologic picture may be spoken of as *primary epithelial hyperplasia* (Figs. 231, a). When the differentiated cells are absent and there remain only the hyperplastic undifferentiated cells of the outer row, the condition may be referred to as *secondary epithelial hyperplasia* (Figs. 231, b). When the line of demarcation between the hyperplastic undifferentiated cells and the stroma is indefinite or absent and the epithelial cells appear in the peri-acinar stroma, the condition may

be spoken of as *tertiary* or *migratory epithelial hyperplasia* (Figs. 231, c, 234, 235).

Primary epithelial hyperplasia represents the usual reaction in chronic mastitis and is not considered to be malignant.

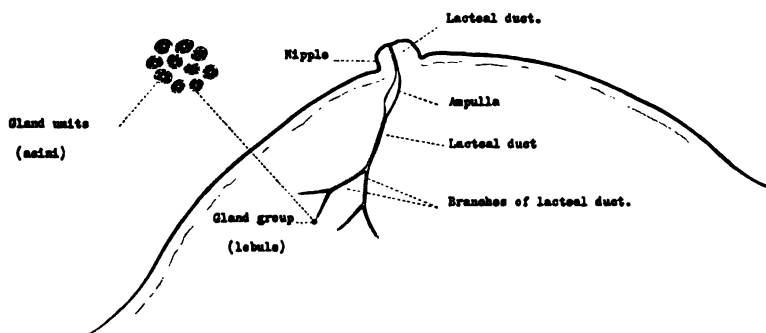


Fig. 230.—Diagram of the mammary gland.



Primary epithelial hyperplasia (not carcinoma).



Secondary epithelial hyperplasia (carcinoma ?).



Tertiary or migratory hyperplasia (carcinoma).

Fig. 231.—Diagram of the mammary acinus in (a) primary, (b) secondary (carcinoma ?) and (c) tertiary or migratory (carcinoma) epithelial hyperplasia.

Tertiary hyperplasia or migratory hyperplasia is the histologic picture of carcinoma.

Secondary hyperplasia is found described as "cystadenoma," "Schimmelbusch's disease," "Reclus' disease," "senile parenchy-

matous hypertrophy," "abnormal involution," etc. It may or may not be malignant; it is placed in a benign group by some authorities and a malignant group by others.

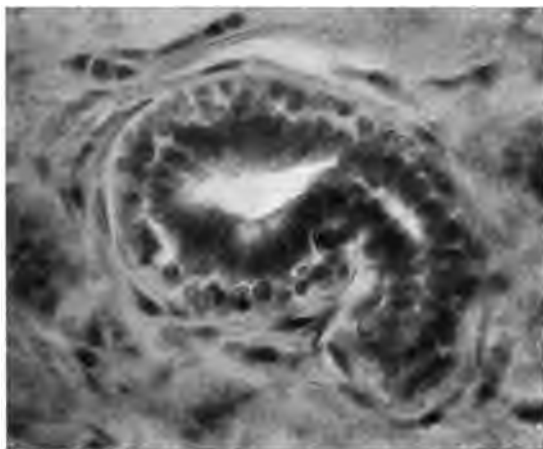


Fig. 232.—Primary epithelial hyperplasia.

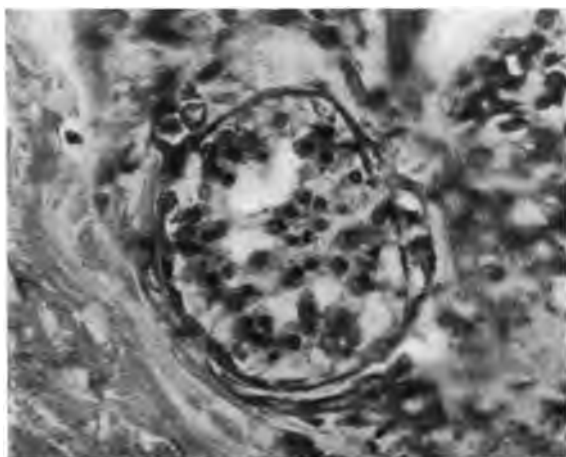
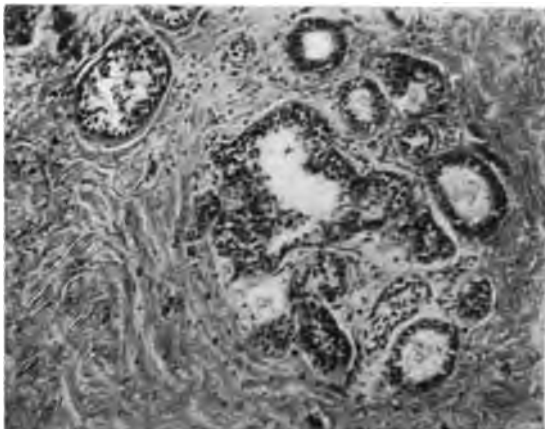


Fig. 233.—Secondary epithelial hyperplasia.

The cells of the epithelium in this condition are often indistinguishable from the cells in tertiary hyperplasia, a characteristic

which arouses a suspicion that the two conditions are intimately related if not a part of the same thing, namely, a malignant hyperplasia.



Figs. 234 and 235.—Tertiary epithelial hyperplasia (carcinoma).

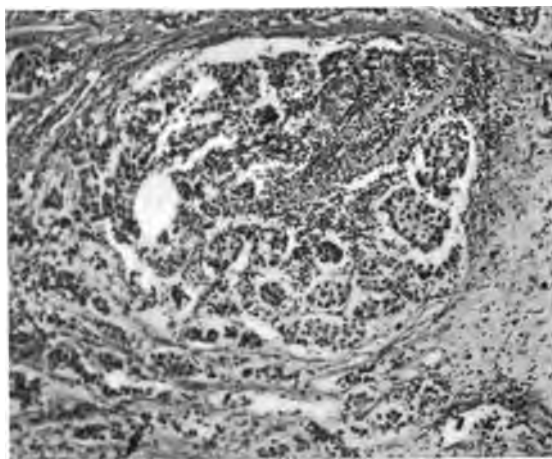


Fig. 236.—Tertiary epithelial hyperplasia (carcinoma).

Without proof relative to the outcome in such a condition, one may state that secondary epithelial hyperplasia is a doubtful

condition, a group which needs special attention during the next decad.

The practical application of a knowledge of the three apparent histologic stages of hyperplasia may readily be seen in the fact that the life-history of the most common pathologic conditions in the breast depends upon epithelial hyperplasia.

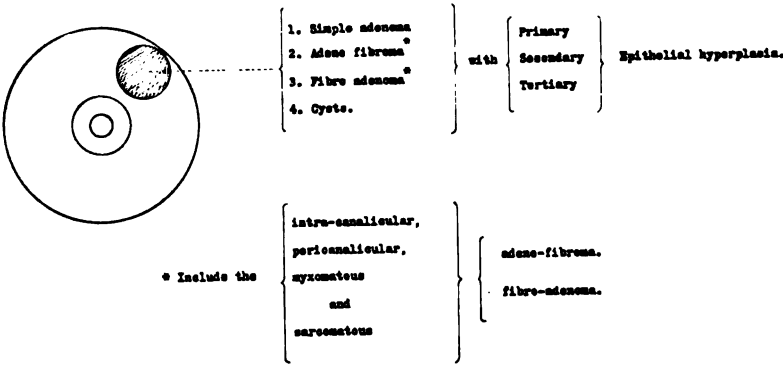


Fig. 237.—Diagram of encapsulated mammary conditions.

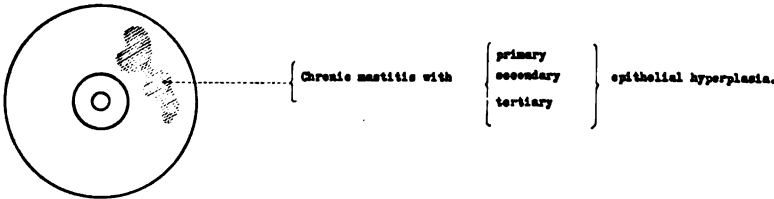


Fig. 238.—Diagrams of non-encapsulated mammary conditions.

Mammary pathologic conditions divide themselves into two groups, *i. e.*, an encapsulated group (Fig. 237) and a non-encapsulated group (Fig. 238).

The encapsulated conditions to which special attention has been given during this investigation are the fibro-epithelial neoplasms, such as simple adenomas, adenofibromas, fibro-adenomas, and cysts, in all of which epithelial hyperplasia occasionally occurs in all three stages.

Of the non-encapsulated conditions, the most common is

chronic mastitis, in which primary, secondary, and tertiary hyperplasias are also frequently found, often in the same field of the microscope.

With the possibility of these conditions being present in cases in which the classic clinical signs of carcinoma are absent, the surgeon and the surgical pathologist must agree upon a scientific histologic standard before any definite operative procedure will bring about scientific knowledge of prognosis.

At present surgeons have no very definite method or standard of dealing with the doubtful group. Radical operations are sometimes done when they are not needed, simply because the surgeon gives the patient the benefit of the doubt. The writer has occasionally seen carcinomas excised for benign tumors.

It seems that there should be a mean between the two extreme conditions, and this mean should, with the aid of a knowledge of the stages of epithelial hyperplasia, serve to solve scientifically the following problems:

1. The percentage of cases of tertiary hyperplasia with or without glandular involvement which may be cured after an arbitrary period of ten years from the time of radical operation.

2. The percentage of cases of secondary hyperplasia which will remain well or recur after the removal of the mammary gland itself, without the removal of the glands, muscles, and large amounts of skin.

3. The percentage of cases with local chronic mastitides or encapsulated conditions which return later, with secondary or tertiary hyperplasia, after local removal.

The question for the surgeon to decide is whether or not he is willing to run the chance of local recurrence after wide local removal of a malignant condition, followed by an extensive operation after microscopic examination, or take the credit of doing radical operations unnecessarily in an attempt toward conservatism.

This, with our present knowledge, can be answered only by conscience and not by scientific data.

The plan which suggests itself to the writer after an extensive



experience with the pathologic conditions to be dealt with, and also an intimate association with the activities of surgeons, seems to be based upon some known factors relative to the histology of epithelial activities, and the fact that surgeons differ regarding the extent of operations necessary in the conditions which have been described above.

1. The conditions which are associated with classic clinical signs of carcinoma should be treated radically.

2. The doubtful cases in women near or over thirty-five years of age should have the entire mammary gland removed for immediate examination. If primary or secondary hyperplasia be present, nothing more should be done; if tertiary hyperplasia be present, a radical operation should be performed.

3. In doubtful patients near or under thirty-five years of age a wide section of the mammary gland, including the pathologic conditions, should be removed for examination. If primary hyperplasia be present, nothing more should be done. If secondary hyperplasia be present, the rest of the mammary gland should be removed, and if tertiary hyperplasia be present, the radical operation should be accomplished.

This plan avoids incision of tumors. It removes the possibility of unnecessary radical operations and their physical and psychic embarrassment. It provides for a scientific means of determining more accurately the stage at which cancer may be cured by surgical operations, and the extent of the operation which is necessary to effect such a cure.

In the experience of this clinic the removal of the mammary gland preceding an immediate radical operation has not been associated with earlier recurrence than has been found after a primary radical operation.

The plan is herewith presented, with the realization that it is a conservative experiment which is based on scientific facts. It is based upon actual research upon each specimen, and is free from the incumbrances of extensive terminology and dogmatism, relative to which specimen is and which is not carcinoma.

It presents a means of actually determining what is clinically malignant.

It makes the surgeon an essential factor in the study of the biology of the epithelial cells and their relation to cancer. It will save many patients from unnecessary mutilation, and will give radicalism its proper place in the treatment of cancer of the breast.

## **DUCTLESS GLANDS**



## THE CLINICAL AND PATHOLOGIC RELATIONSHIP OF SIMPLE AND EXOPHTHALMIC GOITER\*

HENRY S. PLUMMER

Up to January 1, 1909, 1004 operations had been done on 966 cases of goiter at St. Mary's Hospital. A brief review shows that we were classifying the cases as simple and exophthalmic goiter. We recognized that a considerable percentage of cases of so-called simple goiter had constitutional symptoms. Whether or not the cases having constitutional symptoms were placed on the simple or exophthalmic list depended upon how closely the clinical complex approached the well-known picture of Graves' disease.

Wilson, in 1908, after reviewing the available pathologic material from the cases that had been diagnosed exophthalmic goiter, pointed out that 80 per cent. of the glands showed hyperplastic changes, and that in general the length and severity of the case-history could be pointed out from the pathologic findings. While it was impossible to overlook the fact that the tissue removed from the majority of patients having a well-developed picture of Graves' disease was hyperplastic, we could not come definitely to the conclusion that this evidence of activity on the part of the thyroid was a constant finding in exophthalmic goiter as long as 20 per cent. of the cases so diagnosed did not show this change in the thyroid.

At about this time a review of the clinical histories and pathologic findings of the entire series listed as simple and exophthalmic

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goiters led the writer to the following tentative conclusions: (1) That at least two distinct but similar types of thyroid intoxication exist, one associated with non-hyperplastic goiter, the other with hyperplastic or hypertrophic thyroid; (2) that exophthalmos should be noted only in cases having hyperplastic or hypertrophic thyroids; (3) that the failure of our statistics to show the above conclusions was due largely to the following errors: (a) accepting the clinical findings and diagnosis of exophthalmic goiter for all cases placed on the exophthalmic goiter list; (b) accepting the pathologic findings from only a portion of one lobe of the thyroid; (4) that the clinical errors were attributing the tremor, tachycardia, etc., of neurasthenia, cardiovascular and nephritic diseases to the thyroid and noting the existence of exophthalmos when only a Stellwag's sign and naturally prominent eyes are associated with the thyrotoxicosis of non-hyperplastic goiter.

I have from time to time pointed out in discussions statistical data bearing out the above conclusions, but have refrained from publication until going into a wealth of confusing detail to explain the apparent exceptions is unnecessary.

In writing the histories of the 3207 cases that have come to operation since January 1, 1909, forms were used covering the points which might later prove of interest. Figures and signs having, in so far as possible, fixed values, were used in place of descriptive adjectives. Observations of facts and opinions were carefully distinguished. The clinical and pathologic findings were placed in parallel columns without any comparison of notes on the part of the clinicians and pathologists. This made possible the compilation of statistics by clerks who were not in any way warped by preconceived ideas or a knowledge of factors other than those under immediate consideration.

The term thyrotoxicosis is here applied to the constitutional state associated with goiter. As a matter of convenience for quickly presenting the association of the clinical and pathologic findings, the constitutional symptoms accompanying goiter were attributed to a toxemia, the result of a disturbed thyroid function. As a temporary expedient the cases were classified pathologically

as hyperplastic and non-hyperplastic, and clinically as hyperplastic toxic, hyperplastic atoxic, non-hyperplastic toxic, and non-hyperplastic atoxic. The glands showing marked hypertrophy were included with the hyperplastic goiters. Following this classification for the 2917 new cases coming to operation between January 1, 1909, and January 1, 1913, 42.8 per cent. were hyperplastic and 57.2 per cent. were non-hyperplastic. Of the hyperplastics 99.2 per cent. were toxic and 8 per cent. were atoxic. Of the non-hyperplastic, 23.3 per cent. were toxic and 76.7 per cent. were atoxic.

While the association of the constitutional symptoms with non-hyperplastic goiter was to a certain extent a personal equation, this was to a limited degree true for the cases having hyperplastic thyroids. The estimation that 23.3 per cent. of the non-hyperplastic goiters were toxic was made on a conservative basis.

Patients coming under observation with non-hyperplastic toxic goiter gave a history of having first noted the goiter at the average age of 22 years, and the evidence of intoxication at the average of 36.5 years. The corresponding ages for hyperplastic goiter were respectively 32 and 32.9 years.

That non-hyperplastic goiter was noted ten years earlier in life than hyperplastic goiter, that fourteen and one-half years elapsed between the appearance of non-hyperplastic goiter and the development of notable toxic symptoms, and that the constitutional symptoms were noted but a few months later than the goiter in the patients affected with hyperplastic thyroid was alone sufficient to show that we were dealing with at least two distinct pathologic and clinical groups. That one was not the sequence of the other was self-evident.

Are all hyperplastic goiters coming to operation toxic? Throughout the series the number of cases in which the clinician failed definitely to note and attribute constitutional symptoms to the thyroid and which were later diagnosed by the pathologists hyperplastic thyroid varied from 2 cases in 1909 to 4 cases in 1912; 2 of these 4 cases were in children under four years of age and could be excluded in considering the hyperplasia of adults. The third case

was a girl, aged fifteen years, who gave a history of having noticed the goiter, periods of tremor, tachycardia, and palpitation for nine months. However, these symptoms were not attributed to the thyroid previous to operation. The fourth case was a woman, aged forty-seven years, who gave a history of having noticed the goiter for twelve years, rapid growth during the few months previous to coming to operation, and a long train of symptoms, part of which might be attributed to thyroid intoxication. A few cases that had small areas of hyperplasia in the thyroid were excluded because they were still under discussion by the pathologists. The majority of them had moderate toxic symptoms, indicating that the activity of the thyroid was proportionate to the degree of the hyperplasia.

Is hyperplasia of the thyroid more prevalent in the first two decades of life than we have definite knowledge of, perhaps indicating a thyroid activity in response to some demand that cannot be considered far from normal? If so, is this hyperplasia of the thyroid to be sharply distinguished from the hyperplasia associated with Graves' disease, which develops at the average age of thirty-two? I do not believe these questions can be definitely answered at the present time, though there is much evidence suggesting an affirmative answer, at least to the clinical side of the question.

Is the exophthalmos of thyrotoxicosis always associated with hyperplastic goiter? The pathologic reports fail to show the presence of hyperplasia in the cases in which exophthalmos was noted by the clinician 6 times in 1909, 4 times in 1910, twice in 1911, and not in a single instance in 1912. In 1912 there were 911 new cases of goiter that came to operation. In most of the exceptions to the rule previous to 1912, we were able definitely to prove that there was an error in noting the presence of exophthalmos.

Should all toxic hyperplastic goiters be included under the term exophthalmic goiter? Possibly there is a small group of cases which should not be included. However, that there is small chance for error in answering this question in the affirmative if we include only those cases coming to operation is indicated by—



(1) of the cases having diffuse hyperplasia of the thyroid coming under observation from one to three, three to six, six to nine, nine to twelve, twelve to eighteen, eighteen to twenty-four months and over two years from the onset of toxic symptoms respectively, 50, 59, 67, 75, 80, 80, and 87 per cent. had exophthalmos (questionable cases excluded); (2) if we select from any periods in our series 25 consecutive patients having hyperplastic thyroids and mild toxic symptoms, over 50 per cent. have exophthalmos; and if we select from the total number of patients coming to operation during 1911 and 1912 the 25 cases of non-hyperplastic thyroids having the most intense intoxication, exophthalmos is not noted in a single instance. It is quite possible that exophthalmos may be associated with non-hyperplastic toxic goiter, but if so, it is so rare that it must be in a way considered accidental.

Is the symptom-complex accompanying hyperplastic goiter to be directly attributed to disturbed thyroid function? While it has been so considered in this paper only as a matter of convenience for pointing out the association of the clinical and pathologic findings, and while I do not wish to enter into a discussion of this subject at the present time, I wish to call attention to a point in support of this theory that, so far as I know, has not hitherto been made, namely, that an individual, aged twenty-two years, with an adenoma of the thyroid, has a definite chance of developing a train of symptoms during the thirty-sixth year so similar to the symptom-complex associated with hyperplastic thyroid that the best-trained diagnosticians are constantly confusing the two conditions.

Can we associate the symptom-complex of non-hyperplastic toxic goiter with any definite pathologic change in the thyroid? For the present this question must be answered in the negative.

Correlating the above statistical data, we may safely come to the conclusion that exophthalmic goiter is a definite clinical complex always associated with hyperplasia of the thyroid, and that it should be sharply distinguished from the constitutional state or states that may develop with non-hyperplastic goiter. Still more interesting and convincing is the correlation of a mass of

detail with the data given here. This involves too much for a short paper. However, a general conception of the clinical pictures accompanying non-hyperplastic toxic and exophthalmic goiter is given as an introduction to the paper by Drs. Blackford and Sanford.\*

For the purpose of quickly presenting the clinical pictures, let us note the parallelism of thyrotoxicosis and alcoholism and assume that there are three toxic elements in the thyroid secretions, one damaging chiefly the nervous system, one the circulatory system, and the other producing exophthalmos. In exophthalmic goiter all three elements are in excess, but the clinical picture is dominated by a nerve toxin, although in individual cases the circulatory toxin or element producing exophthalmos may seem to be in excess.

The intoxications from non-hyperplastic goiter may be divided into two merging groups: (1) A group in which the cardiac toxin predominates, in which the clinical picture closely resembles and in many instances cannot be differentiated from the cardiovascular complex resulting from alcoholic, luetic, septic, and other well-known toxins; (2) a group more closely approaching the picture of Graves' disease and including the cases that have been erroneously so diagnosed by the mass of the profession.

The average lapse of time between the appearance of non-hyperplastic goiter and toxic symptoms is 14.3 years. That the patient comes under observation three years later indicates that the onset is usually insidious. Nervousness, tremor, loss of strength and weight, as a rule, develop slowly, but may appear suddenly long before definite evidence of myocardial damage. The administration of iodine may cause the sudden appearance of those symptoms with myocardial insufficiency much as they might follow the prolonged drinking bout of an old toper who had not previously shown decided evidence of chronic alcoholism. In some cases the clinical aspect, as noted above, closely approaches that of exophthalmic goiter. However, the symptoms are less complex, less definitely associated, and except for a damaged heart, less intense.

\* A Demonstration of a Depressor Substance in the Serum of the Blood in Exophthalmic Goiter, *Amer. Jour. Med. Sci.*, December, 1913, pp. 796-809.

There is much evidence to suggest that during the 14.5 years previous to the onset of definite toxic symptoms many of the cases of non-hyperplastic thyroid may be compared to the alcoholic tippler in that if the soil is right they develop arteriosclerosis, in many cases showing the combined picture of thyrotoxicosis and arteriosclerosis.

The development of a typical syndrome of Graves' disease in a case having a definite history of simple goiter means that a hyperplastic goiter has been superimposed upon the simple type.

The onset of exophthalmic goiter is, as a rule, relatively acute and the course of the disease fairly definite. The clinical picture early in the history is that of a toxin acting directly on the more vital organs, more notably the central nervous and vascular systems. Later it is made more complex by the interaction of those organs whose functions have been directly disturbed by the toxin. The order of onset of the most important symptoms based on the average of our series is as follows: (1) Cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of strength; (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice; and (13) death.

If the average course of the intoxication be represented by a curve, the greatest height is reached during the latter half of the first year, and then suddenly drops to the twelfth month. In many instances it reaches the normal base-line during the next six months. More often it fluctuates with periods of exacerbation for the next two to four years. Secondary symptoms and exophthalmos may remain, but the active course only rarely continues over four years without distinct intermissions. Compare the striking resemblance of the character, order of onset, and course of this train of symptoms with that resulting from the heavy use of alcohol by a susceptible individual over a corresponding period of time. Near the crest of the curve any shock, operation, etc., that treats the patient to another drink may result in tremens or death.

In the average course after the first year the symptoms that

may be attributed to long-continued intoxication rather than to a high degree of acute intoxication, *i. e.*, those from the more chronic types of heart, liver, and degeneration of the kidney, enter strikingly into the clinical picture. In attempting to construct a composite curve we find that the curves for those symptoms that we can readily attribute to a high degree of immediate intoxication from the thyroid gradually drop while the curves for those findings attributable to a long-continued intoxication of a lower degree gradually rise.

In a later paper I will point out that there is much evidence to suggest that the sudden onset of the toxic symptoms preceded by a period during which the patient is gradually habituated to the disturbed function of a developing hyperplastic thyroid and that following the disappearance of the clinical manifestations of the intoxication, the patient is still taking care of the products of an overactive gland, and if this overactivity, with or without clinical manifestations, continues sufficiently long in an individual prone to arterial degeneration, arteriosclerosis with secondary contracted kidneys, high arterial tension, etc., will ultimately develop. The picture of thyrotoxicosis from both hyperplastic and non-hyperplastic goiters may be compared to that from alcoholism in its various degrees and manifestations varying with the dose, length of administration, and susceptibility of the individual.

While the weight of the evidence seems to indicate that, whatever the primary cause, the symptom-complex of exophthalmic goiter is directly attributable to hyperplasia of the thyroid, I wish to repeat that I have so considered it in this paper only as a matter of interest and convenience in associating the pathologic and clinical findings.

## THE CLINICAL AND PATHOLOGIC RELATIONSHIPS OF HYPERPLASTIC AND NON-HYPERPLASTIC GOITER\*

HENRY S. PLUMMER

The study of the clinical and pathologic relationships of the various types of goiter has of necessity been followed with the greatest interest in the surgical clinics. In a short paper it is impossible to review the various contributions to the subject. The following points, however, may be selected from the work done in these clinics: the clinical classification of the cases of goiter into simple or exophthalmic or equivalent terms, and the pathologic classification of the thyroids removed at operation into those with and those without sufficient hyperplastic or hypertrophic changes to characterize the gland; the recognition of toxic-goiter heart in a certain percentage of cases that are not diagnosed exophthalmic goiter and a less generally well-defined idea that the cardiac damage is only one of the manifestations of a general toxicosis; the finding of hyperplastic changes in from 70 to 90 per cent. of the thyroids removed for exophthalmic goiter, and the occasional presence of hyperplasia in glands removed from patients not having a history of notable toxic symptoms. Wilson, in 1908, after reviewing the available pathologic material from the cases which had been diagnosed as exophthalmic goiter, and in which operation had been done in the Mayo Clinic, pointed out that 80 per cent. of the glands showed hyperplastic changes, and that, in general, the length and severity of the case history could be determined from the pathologic findings.

\* Read in the Section on Practice of Medicine of the American Medical Association, at the Sixty-fourth Annual Session, held at Minneapolis, June, 1913. Reprinted from Jour. Amer. Med. Assoc., August 30, 1913, vol. lxi, pp. 650, 651.

The relative constancy of notable hyperplasia in the thyroids of fully developed exophthalmic goiter, contrasted with the occasional failure to find this pathologic condition in glands removed from patients having an apparently similar clinical picture of this disease, and the rare finding of diffuse hyperplasia without accompanying evidence of thyrotoxicosis, has led to much discussion and conflicting opinion regarding the specificity of this change.

In the latter part of 1908 a review of the clinical histories and the pathologic reports of our entire series listed as simple and exophthalmic goiters led me to the following conclusions: (1) We have at least two distinct, but very similar, types of thyroid intoxication, one associated with non-hyperplastic goiter, the other associated with hyperplastic or hypertrophic thyroid. (2) All cases having thyrotoxic symptoms with notable hyperplastic thyroids should be diagnosed exophthalmic goiter and that cases having thyrotoxic symptoms without notable hyperplastic thyroids should be classified with the cases of toxic-goiter heart, at least until we have still further evidence on which to subdivide these groups.

The main objection to these conclusions was the inability to make the clinical and pathologic diagnoses agree in about 10 per cent. of the cases. The lack of constancy in the clinical and pathologic relationship in mild and atypical cases could be easily explained. Our series, however, included (and I think this was true in other clinics) a number of cases of apparently typical exophthalmic goiter with exophthalmos and a pathologic report of adenoma, colloid goiter, adenomatosis, etc., without hyperplasia. A careful study of these cases demonstrated errors either in noting the presence of exophthalmos or from incomplete pathologic examination in the majority of instances and a probability of errors in the remaining portion.

This led to the use, in writing the histories of the 3207 cases that have come to operation since January 1, 1909, of forms covering in great detail the points which might later prove of use in studying the development and course of thyrotoxicosis and its relation to the pathologic changes in the thyroid. Figures and

signs having, so far as possible, fixed values have been used in place of descriptive adjectives. Observations of fact and opinion have been carefully distinguished. The clinical and pathologic findings have been placed in parallel columns without any comparison of notes on the part of the clinicians and the pathologists. Clinical records for statistical purposes have not been changed after the patient came to operation. This has made possible the compilation of statistics by clerks who are not in any way warped by preconceived ideas or a knowledge of factors other than those under immediate consideration.

Correlating the statistical data, we may safely come to the conclusion that exophthalmic goiter is a definite clinical complex always associated with hyperplasia of the thyroid, and that it should be sharply distinguished from the constitutional state or states that may develop with non-hyperplastic goiter. As a complete review of this material is beyond the scope of a short paper and the patience of the average reader, I have attempted to answer the questions brought up with the least possible amount of statistical data, using only the following factors: the age at which the goiter is first noticed by the patient; the age at which thyrotoxic symptoms developed; the presence or absence of exophthalmos, and the presence or absence of notable hyperplasia in the thyroid. It is my purpose to take up these questions with a full report in a series of papers.

The term "thyrotoxicosis" is here applied to the constitutional state associated with goiter. As a matter of convenience for quickly presenting the association of the clinical and pathologic findings, the constitutional symptoms accompanying goiter have been attributed to a toxemia the result of a disturbed thyroid function. As a temporary expedient the cases have been classified pathologically as hyperplastic and non-hyperplastic, and clinically as hyperplastic toxic, hyperplastic atoxic, non-hyperplastic toxic, and non-hyperplastic atoxic. The glands showing marked hypertrophy have been included with the hyperplastic goiters. Following this classification for the 2917 new cases coming to operation between January 1, 1909, and January 1, 1913, 42.8 per cent. are

hyperplastic and 57.2 per cent. are non-hyperplastic. Of the hyperplastics, 99.2 per cent. are toxic and 0.8 per cent. are atoxic. Of the non-hyperplastics, 23.3 per cent. are toxic and 76.7 per cent. are atoxic.

While the association of the constitutional symptoms with non-hyperplastic goiter involves to a certain extent a personal equation, this is to a very limited degree true for the cases having hyperplastic thyroids. The estimation that 23.3 per cent. of the non-hyperplastic goiters are toxic is made on a very conservative basis.

Patients coming under observation with non-hyperplastic-toxic goiter give a history of having first noted the goiter at the average age of 22 years, and the evidence of intoxication at the average age of 36.5 years. The corresponding ages for hyperplastic goiter are, respectively, 32 and 32.9 years.

That non-hyperplastic goiter is noted ten years earlier in life than hyperplastic goiter, that fourteen and one-half years elapse between the appearance of non-hyperplastic goiter and the development of notable toxic symptoms, and that the constitutional symptoms were noted but a few months (between ten and eleven) later than the goiter in the patients affected with hyperplastic thyroid is alone sufficient to show that we are dealing with at least two distinct pathologic and clinical groups. That one is not the sequence of the other is self-evident.

Are all hyperplastic goiters coming to operation toxic? Throughout our series the number of cases in which the clinician failed definitely to note and attribute constitutional symptoms to the thyroid and which were later diagnosed hyperplastic goiter by the pathologists vary from two cases in 1909 to four cases in 1912. Two of these latter four cases were in children under four years of age and can be excluded in considering the hyperplasia of adults. The third case was that of a girl fifteen years of age who gave a history of having noticed the goiter, periods of tremor, tachycardia, and palpitation for nine months. These symptoms, however, were not attributed to the thyroid previous to operation. The fourth case was that of a woman forty-seven years of age who gave a history of having noticed the goiter for twelve years, rapid



growth during the few months previous to coming to operation, and a long train of symptoms, part of which might be attributed to thyroid intoxication. I have excluded a few cases that had small areas of hyperplasia in the thyroid because they are still under discussion by the pathologists. The majority of them had moderate toxic symptoms, indicating that the activity of the thyroid is proportionate to the degree of the hyperplasia.

Is hyperplasia of the thyroid more prevalent in the first two decades of life than we have definite knowledge of, perhaps indicating a thyroid activity in response to some demand that cannot be considered far from normal? If so, is this hyperplasia of the thyroid to be sharply distinguished from the hyperplasia associated with exophthalmic goiter which develops at the average age of thirty-two? I do not think that we can definitely answer these questions at present, though there is much evidence suggesting an affirmative answer, at least to the clinical side of the question.

Is the exophthalmos of thyrotoxicosis always associated with hyperplastic goiter? The pathologic reports fail to show the presence of hyperplasia in the cases in which exophthalmos was noted by the clinician, six times in 1909, four times in 1910, twice in 1911, and not in a single instance in 1912. Nine hundred and eleven new cases of goiter came to operation in 1912. In most of the exceptions to the rule previous to 1912 we have been able definitely to prove that there was an error in noting the presence of exophthalmos.

Should all toxic-hyperplastic goiters be included under the term "exophthalmic goiter"? Possibly there is a small group of cases which should not. That there is very little chance for error, however, in answering this question in the affirmative if we include only those cases coming to operation is indicated by the following facts: (1) Of the cases having diffuse hyperplasia of the thyroid coming to observation from one to three, three to six, six to nine, nine to twelve, twelve to eighteen, eighteen to twenty-four months, and over two years from the onset of toxic symptoms, 50, 59, 67, 75, 80, 80, and 87 per cent., respectively, had exophthalmos (questionable cases excluded); (2) if we select from any period

ten years of age. One of these cases was operated on in 1906, one in 1909, one in 1911, and two in 1912. In a brief review of the literature on this subject for the past ten years it was possible to find mention of only four cases, and the description of these was too short and void of detail to make them valuable for statistical data. The following are histories of the five cases noted above:

CASE 1.—P5318. Female, aged seven. Date of examination, July 18, 1906. The goiter and eye symptoms had appeared two years previously, and at the same time moderate dyspnea on exertion, as well as tremor. The pulse had ranged from 100 to 130. The child had been growing rapidly, but there had been no appreciable loss of weight or strength. At the time of examination she presented a marked exophthalmos, pulse 120, and a heart dilated possibly one-half inch beyond normal. There were no definite manifestations of nervousness. July 21, 1906: excision of right lobe of thyroid was followed by steady improvement and recovery, the pulse becoming normal and intoxication disappearing.

CASE 2.—A20663. Female, aged four. Date of examination, February 26, 1909. The parents had noticed a mental irritability for eighteen months; while exophthalmos had been remarked twelve to fourteen months previously. There had been no cardiac features and the goiter had not been noted, although a somewhat unusual perspiration had been present. March 5, 1909: both superior thyroid vessels were ligated. This was followed by a subsidence of all the symptoms.

CASE 3.—A57557. Female, aged seven. Date of examination, August 16, 1911. Goiter had been definitely present four months ago, at which time the eyes were large, although photographs showed an enlargement of the eyes for two years. Mental irritability and tremor had been observed, and the pulse had ranged from 130 to 150. No cardiac distress, no loss of weight or strength. On examination, distinct thrills and bruits in the superior thyroid vessels were noted. Exophthalmos was decided, but no cardiac enlargement. August 31, 1911: the left superior thyroid artery was ligated; on September 6, 1911, the right lobe and isthmus were resected. There was a prompt return to normal within a short time.

CASE 4.—A61095. Female, aged eight. Date of examination, November 11, 1911. Three months previous to examination

the patient had had an attack of tonsillitis with vomiting. At that time the eye symptoms were first noted; but no other subjective symptoms. On examination the child was irritable, with a distinct tremor; pulse about 130. No activity in thyroid vessels and no cardiac or muscle damage apparent. February 9, 1911: the left superior vessel was ligated; and on March 14, 1911, the right superior was ligated. Within three days the patient developed a mild attack of scarlet fever, which caused no apparent physical disturbance and did not interfere with an uninterrupted recovery.

CASE 5.—A74040. Female, aged seven. Date of examination, September 9, 1912. Goiter and exophthalmos had appeared one year previous to examination, together with a pulse of 140. No other subjective features. There were marked thrills and bruits in both superior thyroid vessels. October 2, 1912: these vessels were ligated, resulting in a rapid disappearance of the intoxication.

In each of these cases there was a firm, noticeably enlarged thyroid, apparently hyperplastic to the touch. These patients still have full eyes and the thyroid is still large.

In considering these cases in early childhood one naturally compares them to the ordinary case of hyperthyroidism in the adult. In the latter the nervous, cardiac, and muscular systems are more or less involved—a pronounced case generally showing marked damage in each system. In fact, there are few conditions in the adult which produce such wide-spread destruction as an advanced hyperthyroidism.

Plummer's\* observation of the appearance of symptoms in adult exophthalmic goiter is as follows: (1) Cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of muscular strength; (7) loss of weight; (8) cardiac insufficiency; (9) exophthalmos; (10) diarrhea; (11) vomiting; (12) mental depression; (13) jaundice; (14) death.

The following symptoms were noted in the above cases: vasomotor disturbance of the skin in one, tremor in three, mental

\* Plummer: Amer. Jour. Med. Sci., December, 1913, pp. 790-796.

irritability in four, tachycardia in five, exophthalmos in five. All the other features observed in the above table for adults were lacking in this group, or present to so slight an extent as to be insignificant. All the children were able to participate in the vigorous activities of their associates without apparent cardiac or muscular distress, while none of them even approached the crisis so frequently occurring in adults.

The average adult who has progressed as far as marked tachycardia and exophthalmos has developed such evidences of nerve, heart, and muscle damage as to be obviously incapacitated. In the average adult the hyperthyroidism reaches its climax in about nine months. The average length of hyperthyroidism in this group of cases is 11.8 months, or sufficient time in the adult to have produced serious disturbances. Whether this difference of intoxication in the adult and the child is due to a qualitative difference in thyroid activity, to a higher resistance on the part of the child's vascular and nervous mechanism, or to some obscure internal glandular compensation, we have at present no means of determining.

As has been stated, a double ligation was performed on three of these patients; in two a portion of the thyroid was resected, one being preceded by a single ligation, all of which operations gave prompt and, to date, satisfactory results, in contradistinction to adults, most of whom do not seem to be safe without a thyroidec-tomy. In the latter, recurrences are very apt to occur within a comparatively short time after ligation unless a portion of the gland is later removed.

It will be noted that these patients were all females, and it will be interesting to follow up these cases to know if any further activity will be manifested at puberty or later during a pregnancy, the times when hyperthyroidism so frequently begins.

# THE IODIN CONTENT OF THE THYROID, WITH ESPECIAL REFERENCE TO THE PATHO- LOGIC TYPES AND A REVIEW OF SOME EXPERIMENTAL WORK \*

ERNEST V. SMITH, ASSISTED BY A. C. BRODERS

For many years it has been known that the normal thyroid contains a small amount of iodine in combination with a protein or albuminous substance.

The object of this paper is to present a study of the iodine content of toxic thyroids, as observed in the normal and pathologic glands removed at autopsy and in the pathologic glands removed at operation in the Mayo Clinic, and also to review some experimental work pertaining to the metabolic function of this gland.

The results of nearly 200 iodine determinations which have been made agree in general with the results which have been obtained by others who have worked along this same line. Wherein our results differ from the usually accepted findings will be shown by a comparison of the data. The same method of determining the iodine content was used which Hunter advocates, and the precautions which he mentions in his original article on the subject were observed. In all of these iodine determinations blank controls were run with each analysis, and every analysis represents the average of from 2 to 6 tests on the same gland. Every precaution was taken in the preparation of the desiccated thyroid. The glands were finely minced within a few minutes following their removal. When it was not desired to use the entire gland, repre-

\* Read in the Section on Pathology and Physiology of the Amer. Med. Assoc., at the Sixty-fourth Annual Session held at Minneapolis, June, 1913. Reprinted from Jour. Amer. Med. Assoc., January 10, 1914, pp. 113-116.

sentative parts were taken. These portions were dried to a constant weight and powdered fine enough to pass through an eighty-mesh sieve.

A brief outline of the Hunter method is as follows:

One gram of desiccated thyroid gland is mixed in a nickel crucible of about 125 c.c. capacity with 15 gm. of a mixture composed of 138 parts by weight of anhydrous potassium carbonate, 106 parts of anhydrous sodium carbonate, and 75 parts potassium nitrate, and an additional 5 gm. of this fusion mixture spread evenly over the surface. The crucible is then heated over a free Bunsen flame until no further carbonization is observed; it is cooled and the friable residue dissolved in about 150 c.c. of distilled water. To this solution contained in an Erlenmeyer flask of about 500 c.c. capacity is added approximately 50 c.c., or its equivalent, of fresh liquor sodæ chlorinatæ, U. S. P. (containing 2.4 weight per cent. of chlorin). The mixture is then treated with enough phosphoric acid (1 volume of the 85 per cent. syrup and 1 volume of water) to produce a marked yellow tint of free chlorin, an additional 10 c.c. of the phosphoric acid is then added, and the contents of the flask boiled for about one-half hour or until the volume has been reduced to about 150 c.c. The liquid is cooled, 10 c.c. of 1 per cent. aqueous potassium iodid solution is added, and the liberated iodine titrated with  $\frac{200}{N}$  sodium thiosulphate, adding starch paste as the indicator just before the end of the reaction. The  $\frac{200}{N}$  sodium thiosulphate may be made by diluting 25 c.c. of exactly  $\frac{10}{N}$  thiosulphate to 500 c.c.; it changes strength rapidly, and should be prepared fresh at each time determinations are made. One cubic centimeter of  $\frac{200}{N}$  thiosulphate corresponds to 0.0001058 gm. iodine derived from the sample of thyroid used.

Usually it is true that the iodine content of the normal thyroid is the greatest; the content of the colloid gland is less and that of the parenchymatous hypertrophic and hyperplastic gland is least per gram weight of dried gland. Roughly estimated, the normal thyroid will contain about 2.5 mgm., the colloid gland about 1.5 mgm., and the hyperplastic glands about 0.5 mgm. of iodine per gram weight of dried gland.

An analysis of the iodine determinations which were made from 49 glands removed in the surgical treatment of Graves' disease is presented in this article. The parenchymatous hypertrophic and hyperplastic glands are classified in three groups (A, B, and C), A and B being those glands which show very marked hypertrophy and hyperplasia and C being those glands which show regression stages with a greater amount of more or less densely staining colloid.

This histologic classification is from that proposed by Wilson.

The chemical study was completed without a knowledge of the histologic classification in order that there might be no possibility of a biased finding.

TABLE I.—EXOPHTHALMIC GOITERS OF GROUPS A AND B (PARENCHYMATOUS HYPERTROPHY AND HYPERPLASIA) ON WHICH IODIN DETERMINATIONS WERE MADE

Op. No.	SEX	AGE	DATES OF LITIGATIONS	DATE OF OPERATION	WEIGHT	AMOUNT	DENSITY	DIAGNOSIS	GROUP	AMOUNT OF IODIN
65655	F.	27	2/5/12	8/7/12	160	2	2	P.h. and h.	B	0.23
65375	F.	32	3/28/12	7/25/12	130	3	2	P.h. and h.	B	0.66
66360	F.	35	4/15/12, 4/20/12	10/21/12	40	1	2	P.h. and h.	B	0.20
66872	F.	27	4/23/12, 5/1/12	11/4/12	50	1	1	P.h. and h.	B	0.12
67290	F.	26	5/4/12, 5/14/12	10/24/12	100	2	2	P.h. and h.	B	0.28
67491	F.	20	5/11/12, 5/16/12	9/24/12	50	2	2	P.h. and h.	B	0.90
67993	M.	17	6/1/12, 6/8/12	10/3/12	110	3	1	P.h. and h.	B	0.26
68459	F.	19	..	6/6/12	80	2	2	P.h. and h.	B	0.25
68720	F.	34	6/17/12	10/8/12	45	3	1	P.h. and h.	B	0.28
69198	F.	50	6/9/12, 7/4/12	10/2/12	75	3	1	P.h. and h.	B	0.15
68208	*F.	22	..	7/22/12	60	3	3	P.h. and h.	A	1.17
70259	F.	35	7/25/12, 8/6/12	11/11/12	70	1	1	P.h. and h.	B	0.38
74094	F.	48	10/1/12	10/8/12	20	2	1	P.h. and h.	B	0.41
49547	F.	18	10/2/12	10/9/12	55	3	2	P.h. and h.	B	0.88
74127	M.	43	10/3/12	10/10/12	30	3	1	P.h. and h.	B	0.57
74735	F.	30	..	10/19/12	40	2	2	P.h. and h.	B	0.73
75124	F.	26	10/28/12	11/6/12	40	2	2	P.h. and h.	B	1.27
75531	F.	18	11/7/12	11/15/12	40	1	2	P.h. and h.	B	0.80
75743	F.	29	11/11/12	11/15/12	75	1	1	P.h. and h.	B	0.48
75733	F.	31	..	11/12/12	50	2	2	P.h. and h.	B	0.92

\* Designates the specimen belonging to group A. The others belong to group B.

As will be seen from a study of tables I and II, 20 of the 49 glands of the parenchymatous hypertrophic and hyperplastic class are of the groups A and B (early and advanced parenchymatous hypertrophy and hyperplasia). The average iodine content of these 20 glands is 0.54 mgm. per gram weight of dried gland. The smallest amount of iodine found in any of these markedly hyperplastic glands was 0.12 mgm. per gram weight of dried gland. The largest amount was 1.27 mgm. There were 29 glands of the hyperplastic type, which histologically are classified in group C (regressing parenchymatous hypertrophy and hyperplasia). The average iodine content for this group is 1.52 mgm. of iodine per gram weight of dried gland. The smallest amount of iodine found in any gland of this group was 0.44 mgm. per gram of dried gland, and the largest amount was 4.79 mgm. It is among

the glands found in this group that our findings differ from the results as recorded by Marine and Lenhart, working along this same line. From table II it is noted that there are three cases in which the iodine content was found to be well above that which is generally accepted to be the average amount found in the normal thyroid, and there are 16 cases which show an amount above 1.30 mgm., which is usually accepted as the minimum for normal thyroids. In other words, about 33 per cent. of hyperplastic glands show a high iodine content.

TABLE II.—SHOWING A LIST OF EXOPHTHALMIC GOITER OF GROUP C (PARENCHYMATOUS HYPERTROPHY, HYPERPLASIA, AND REGRESSION) ON WHICH IODINE DETERMINATIONS WERE MADE

OP. No.	SEX	AGE	DATES OF LIGATIONS	DATE OF OPERA- TION	SECRETION			DIAGNOSIS	GROUP	AMOUNT OF IODINE
					Weight	Amount	Density			
64836	F.	44	3/7/12, 3/12/12	7/3/12	100	2	2	P.h. and h. + R.gs.	C	0.44
67571	F.	41	5/15/12, 5/23/12	8/28/12	50	3	3	P.h. and h. + R.gs.	C	1.33
67693	F.	28	5/18/12, 5/28/12	10/1/12	90	3	3	P.h. and h. + R.gs.	C	1.64
68578	F.	32	6/1/12, 6/6/12	11/6/12	80	3	3	P.h. and h. + R.gs.	C	1.21
68590	F.	28	6/4/12, 6/10/12	9/4/12	50	3	3	P.h. and h. + R.gs.	C	0.46
68790	F.	43	6/20/12	10/7/12	50	2	2	P.h. and h. + R.gs.	C	0.49
69368	F.	20	7/1/12, 7/8/12	11/1/12	120	3	3	P.h. and h. + R.gs.	C	1.34
70458	F.	34	7/18/12	12/20/12	70	3	3	P.h. and h. + R.gs.	C	0.46
70539	M.	38	7/26/12	10/24/12	35	3	3	P.h. and h. + R.gs.	C	1.12
70621	F.	51	7/31/12, 8/ /12	12/11/12	70	2	2	P.h. and h. + R.gs.	C	0.45
72542	F.	38	8/28/12	9/4/12	40	2	2	P.h. and h. + R.gs.	C	0.53
73226	F.	39	9/10/12, 9/19/12	10/10/12	90	3	3	P.h. and h. + R.gs.	C	1.18
73217	F.	36	9/16/12	9/24/12	47	3	3	P.h. and h. + R.gs.	C	1.29
73011	F.	34	9/18/12	9/24/12	35	3	4	P.h. and h. + R.gs.	C	4.74
73815	M.	29	9/25/12	10/3/12	100	3	3	P.h. and h. + R.gs.	C	1.72
73863	F.	42	9/27/12, 10/5/12	10/10/12	25	3	3	P.h. and h. + R.gs.	C	1.62
73616	F.	32	10/1/12, 10/7/12	Aut. 175	...	4	4	P.h. and h. + R.gs.	C	4.79
73982	M.	...	...	Aut. 170	...	3	3	P.h. and h. + R.gs.	C	2.18
74095	M.	18	10/7/12, 10/14/12	2/1/13	30	3	3	P.h. and h. + R.gs.	C	2.18
74284	F.	23	10/9/12	10/19/12	50	3	3	P.h. and h. + R.gs.	C	1.65
74930	F.	29	10/18/12	10/28/12	45	2	3	P.h. and h. + R.gs.	C	1.51
74909	F.	26	10/18/12	10/28/12	80	3	3	P.h. and h. + R.gs.	C	1.65
74873	F.	34	...	10/19/12	30	2	2	P.h. and h. + R.gs.	C	0.99
74929	...	35	10/30/12	11/7/12	50	2	3	P.h. and h. + R.gs.	C	1.24
75164	F.	39	10/30/12	11/6/12	45	3	3	P.h. and h. + R.gs.	C	1.66
75498	M.	26	11/2/12	11/2/12	90	3	3	P.h. and h. + R.gs.	C	1.46
75496	M.	30	11/8/12	11/15/12	90	4	3	P.h. and h. + R.gs.	C	1.94
76959	F.	35	...	12/11/12	65	2	3	P.h. and h. + R.gs.	C	1.87
77136	F.	34	12/14/12	12/20/12	50	3	2	P.h. and h. + R.gs.	C	1.09

Many of the glands analyzed for iodine were from patients who had a ligation previous to the time of removal of the gland. The question naturally arises, Did the ligation affect the iodine content? From the chart showing thyroids of groups A and B,—those repre-



senting early and marked hypertrophy and hyperplasia,—it is noted that there are only four patients who were not ligated previous to operation. The average iodine content from these four patients is found to be 0.77 mgm. The average iodine content for the 16 patients who had been ligated shows 0.49 mgm. The glands of these groups then show a loss in the iodine content following ligation.

The same condition is found to be true in the glands listed in group C. There are 29 glands of this group on which iodine determinations have been made. Only three from this group have not had ligations previous to removal. The average iodine content of these three glands is found to be 1.68 mgm., while the content of the 26 glands of this group which had a previous ligation shows an *average* iodine content of 1.5 mgm. When the iodine content of the whole class of hyperplastic glands is considered and the content of the non-ligated glands compared to the content of those which have had a previous ligation, it is found that the average for the non-ligated glands is slightly below those which have been ligated.

It is our opinion, from a study of the above data, that ligation in the majority of cases slightly decreases the iodine content of hyperplastic glands. It is true that the averages of the non-ligated cases are computed from a small number. However, it is significant that the results are similar in both groups of cases.

Does age play any part in the amount of iodine found in the hyperplastic gland? Ten patients, who were between seventeen and thirty years of age, show an average iodine content of 1.02 mgm. Ten patients, who were all above thirty years of age, showed an average iodine content of 0.71 mgm. It is evident from these figures that hyperplastic glands of patients from thirty to fifty years of age contain less iodine per gram weight than do those glands from patients of fifteen to twenty-five years of age.

The size of the hyperplastic gland also seems to bear some relation to the amount of iodine per gram weight of dried gland. The larger glands of group C are found to have less iodine per gram of dried gland than the smaller glands. An average of 11 of the larger glands of group C shows 1.37 mgm. of iodine as compared with

1.59 mgm., the average of 11 small glands. The same condition also exists in the case of glands of groups A and B. Averages on eight large and a like number of small glands from these groups show the amount of iodine as 0.33 mgm. in case of the large glands, as compared to 0.56 mgm. in case of small glands.

In considering the amount of iodine found in the thyroid, at least two factors regarding the nature of the colloid substance must be considered. The first factor of importance is the *amount* of colloid. The second factor is the *density* of the colloid. There are certain hyperplastic glands which have large acini, filled with a thin or watery secretion, which do not have as great an iodine content as some other glands whose acini may not be so large but whose secretion is denser. As a rule, the denser the secretion, the deeper it stains and the larger amount of iodine it contains.

The iodine determinations of 17 simple colloid goiters classified in group H (colloid thyroids) show an average iodine content of 1.84 mgm. of iodine per gram weight of dried gland. The minimum amount found in any of the colloid glands was 0.41 mgm. per gram weight and the maximum amount was 3.33 mgm. These variations are about the same as those found by Marine and Lenhart, except that both our maximum and minimum are slightly below what they found.

It is usually found that the pure fetal adenomas contain very small amounts of iodine. This is to be expected, as the colloid in such glands is small in amount and rarely of much density, as shown by its staining reaction.

In connection with this work on the iodine content of the thyroid as found in pathologic specimens I have carried out a series of experiments on dogs to determine to what extent the iodine content of their thyroids would be affected by the administration of the iodids, and which form of medication would produce the greatest increase in iodine content.

Fourteen dogs have been used in these experiments. In selecting the dogs, endeavor was made to obtain dogs as near the same size and weight as possible. Previous to the time of beginning the experiments they were kept under the same conditions as

to housing and feeding. During the period of administration of iodids the dogs were kept and fed under the same conditions. The methods of administration of iodids were as follows:

1. The painting of the U. S. P. tincture of iodine on the shaven skin.

2. The administration, by mouth with the food, of a 1:1 aqueous solution of potassium iodide in doses ranging from 15 to 30 drops each day.

3. The subcutaneous injection of 20 to 45 drops of a 1:1 solution of potassium iodide diluted to 5 c.c., one injection each day.

Three dogs of the entire number were used as controls, and to these no iodids were given. The determination of the iodine content of the thyroids removed from the three control dogs was 2.58 mgm. of iodine per gram weight of dried gland. Five dogs were painted with the tincture of iodine, and the average iodine content of these glands was 6.5 mgm. per gram weight of dried gland. Three dogs had subcutaneous injections of potassium iodide. The average iodine content of their glands was 5.53 mgm. Four dogs were given potassium iodide with their food. The average iodine content of their glands was 2.73 mgm.

TABLE III.—SHOWING THE STORAGE POWER OF THE THYROID GLANDS OF DOGS REGARDING IODINE

No. of Dog	TREATMENT	NUMBER OF TREATMENTS	DOSE GIVEN	DATE OF REMOVAL	AMOUNT OF IODINE PER GRAM
1	None.	0	0	8-4-12	2.50 mgms.
4	None.	0	0	8-28-12	3.86
7	None.	0	0	8-15-12	1.40
2	KI with food.	5	45M	8-15-12	1.61
11	KI with food.	10	30M	10-28-12	1.47
12	KI with food.	14	35M	10-28-12	5.10
5	KI injected.	7	15	8-28-12	5.30
8	KI injected.	7	15	9-17-12	3.54
14	KI injected.	16	30	11-20-12	7.86
3	Tinct. iodine painted.	5	4" x 5"	8-15-12	5.57
6	Tinct. iodine painted.	7	4" x 5"	8-28-12	5.43
9	Tinct. iodine painted.	7	4" x 5"	9-16-12	7.66
10	Tinct. iodine painted.	11	4" x 6"	10-28-12	3.64
13	Tinct. iodine painted.	16	8" x 8"	11-20-12	10.18

It was noted from these methods of administration that the external application of the tincture of iodine caused the greatest average increase of the iodine content of the gland. It was further noted that the dogs receiving the subcutaneous injection of the iodide lost weight very rapidly. While these dogs did not store up as much iodine in their thyroids as the dogs which were painted with the tincture, yet they seemed to experience a much greater systemic effect from the drug. When the potassium iodide was fed with the food, it caused very little increase in the iodine content.

Pathologists doing postmortems often see the final picture in the most extreme cases of hyperthyroidism, and it is from such cases and from a review of all the cases which have come to autopsy that three most constant conditions are encountered.

First: The extreme emaciation of all patients dying from hyperthyroidism is mentioned. That the iodides, when given in large doses over a period of time, do cause a great loss in body weight there is no doubt. The same therapeutic fact is taken advantage of by manufacturers of proprietary antifat remedies, and preparations of thyroid are greatly used by them.

Second: The general appearance which the intestinal tract presents is noted, *i. e.*, the contracted intestines, which have a congested appearance with the mesenteric vessels engorged with blood—such a condition may be produced by chronic poisoning with any of the metallic poisons. A similar condition has been noted in animals which we have sacrificed after chronic iodine poisoning.

Third: The microscopic picture of a section of the liver. Almost invariably the section shows fatty degeneration (lipoid changes) of various degree. This lipoid change of the liver is the result of some chronic intoxication. The question naturally arises, What is the nature of the poison producing it? It is well known that such fatty changes occur in many chronic diseases. Tuberculosis and chronic alcoholism might be cited as examples in which such a change frequently occurs. It has been known for many years that phosphorus will produce a lipoid change of the liver when given in toxic doses. Will iodine also produce such a

lipoid change when so given? Cushny says that iodine, like phosphorus, does produce a fatty degeneration (or lipoid change) in the liver and other organs. Further, he says that thyroid likewise produces a fatty degeneration in various organs when given in excessive doses to the point of poisoning.

A poison known as acetonitril has been used by Hunt as a measure to determine thyroid activity. He found that by feeding white mice with cracker cakes containing desiccated thyroid, their resistance to acetonitril poisoning was increased.

Following Hunt's plan, I have carried out a series of experiments on white mice, feeding them with the desiccated thyroid of parenchymatous hypertrophic and hyperplastic and colloid glands removed at operation. Cracker cakes were used as a food for the controls, and cracker cakes, to which the fresh desiccated glands were added, were used as a food for experiment. It was found that those mice which received the cracker cakes containing the desiccated parenchymatous hypertrophic and hyperplastic glands have a slightly greater resistance to acetonitril than those mice which were fed on the plain cracker cakes. Those mice fed with cracker cakes to which the desiccated colloid goiters had been added had a higher resistance than either the controls or those fed with hyperplastic glands. In neither group was it possible to produce a resistance equal to that produced by Reid Hunt when he fed the desiccated commercial thyroid made from the sheep.

However, by painting the tails of the mice with tincture of iodine on three or four successive days, it was found that an increase in resistance to acetonitril poisoning was obtained equal to, and in many cases greater than, that obtained by feeding with desiccated thyroids. When the painting is carried beyond the seventh or eighth day, the degree of resistance becomes less positive, due to the poisonous effects produced by the iodine.

Regarding chronic iodism in man, the United States Dispensary gives the following symptoms: "Even in medicinal doses, it sometimes causes alarming symptoms, such as fever, restlessness, disturbed sleep, palpitations, excessive thirst, acute pain in the stomach, vomiting and purging, violent cramps, frequent pulse,

MOUSE NUMBER	METHOD OF FEEDING	NUMBER OF DAYS FED	IODIN CONTENT OF SUBSTANCE MIXED WITH CRACKER CAKES	WEIGHT OF GLAND IN EACH CRACKER CAKE	DATE OF TEST	GRAM WEIGHT OF MOUSE	DOSE IN MILLIGRAMS ACETONITRIL	DOSE PER MOM. OF MOUSE	RESULTS: + Died, 0 Lived
1a	Plain cracker cakes.	20	Fed on plain cracker cakes.	Absent	1912 8-3	20.6	6.66	0.32	0
2a	" " "	20	" " " "	"	9-14	17.6	7.04	0.4	0
3a	" " "	20	" " " "	"	9-14	16.6	8.30	0.5	0
4a	" " "	20	" " " "	"	9-20	18.7	9.83	0.525	0
5a	" " "	20	" " " "	"	9-20	17.0	9.35	0.55	0
6a	" " "	20	" " " "	"	9-20	19.1	10.98	0.575	+
7a	" " "	20	" " " "	"	9-14	17.4	10.44	0.6	+
8a	" " "	20	" " " "	"	8-3	23.3	16.19	0.7	+
9a	" " "	18	" " " "	"	8-17	15.7	9.42	0.6	+
10a	" " "	20	" " " "	"	8-14	17.3	12.11	0.7	+
1b	Desiccated Exop. fed with crackers.	20	0.5 mgm. of iodine per gm. weight of gland used. Gland taken from Class B. P.h. and h.	0.3 gm. in each cracker fed. One cracker weighed 4 gm.	9-12	16.0	9.60	0.6	0
2b	Desiccated Exop. fed with crackers.	20	0.5 mgm. of iodine per gm. weight of gland used. Gland taken from Class B. P.h. and h.	0.3 gm. in each cracker fed. One cracker weighed 4 gm.	9-12	25.3	15.30	0.6	0
3b	Desiccated Exop. fed with crackers.	21	0.5 mgm. of iodine per gm. weight of gland used. Gland taken from Class B. P.h. and h.	0.3 gm. in each cracker fed. One cracker weighed 4 gm.	9-21	26.3	16.98	0.6	0
4b	Desiccated Exop. fed with crackers.	21	0.5 mgm. of iodine per gm. weight of gland used. Gland taken from Class B. P.h. and h.	0.3 gm. in each cracker fed. One cracker weighed 4 gm.	9-21	22.4	15.68	0.7	+
5b	Desiccated Exop. fed with crackers.	20	0.5 mgm. of iodine per gm. weight of gland used. Gland taken from Class B. P.h. and h.	0.3 gm. in each cracker fed. One cracker weighed 4 gm.	9-20	18.3	10.98	0.6	+
1c	Desiccated colloid. Class H. Fed with cracker cakes.	14	Average 1.5 milligrams.	0.3 gm. in each cracker fed.	9-16	21.9	15.53	0.7	0
2c	Desiccated colloid. Class H. Fed with cracker cakes.	20	Average 1.5 milligrams.	0.3 gm. in each cracker fed.	9-12	15.5	14.40	0.8	0
3c	Desiccated colloid. Class H. Fed with cracker cakes.	21	Average 1.5 milligrams.	0.3 gm. in each cracker fed.	9-21	21.3	19.17	0.9	+
4c	Desiccated colloid. Class H. Fed with cracker cakes.	20	Average 1.5 milligrams.	0.3 gm. in each cracker fed.	9-12	18.5	20.4	1.1	+
1dg	Painted with Tr. I.	4X	Fed on plain cracker cakes.	Absent	10-8	19.4	11.64	0.6	0
2dg	" " "	4X	" " " "	"	10-8	17.2	12.04	0.7	0
3dg	" " "	4X	" " " "	"	10-8	18.8	15.04	0.8	0
4dg	" " "	4X	" " " "	"	10-8	24.4	24.40	1.0	+
5dg	" " "	4X	" " " "	"	10-4	18.1	18.10	1.0	0
6dg	Control.	0	" " " "	Control	10-4	20.0	10.00	0.5	+
7dg	"	0	" " " "	"	10-8	18.2	9.10	0.5	0
8dg	"	0	" " " "	"	10-8	20.4	12.24	0.6	+
9df	Painted with Tr. I.	8X	" " " "	Absent	9-22	14.7	14.70	1.0	0
10df	"	8X	" " " "	"	9-22	17.7	31.86	1.8	0
11df	Control.	0	" " " "	Control	9-23	15.2	12.16	0.8	+
12de	"	0	" " " "	"	9-27	21.1	12.66	0.6	+
13de	"	0	" " " "	"	9-27	13.6	10.88	0.8	+
14de	Painted with Tr. I.	7X	" " " "	Absent	9-27	17.2	17.20	1.0	0
15de	"	7X	" " " "	"	9-27	15.1	15.23	1.1	0
16de	"	7X	" " " "	"	9-27	16.9	21.90	1.3	+
17de	"	7X	" " " "	"	9-27	14.0	28.00	2.0	+

and, finally, progressive emaciation if the medicine be not laid aside. Absorption of the mamma and wasting of the testicle have been reported as caused by the long-continued use of the drug." It will be noted that many of the symptoms present in chronic iodism correspond very closely to those of hyperthyroidism.

Clinical experience regarding the use of iodids in simple goiter demonstrates that there is a certain class of patients who often receive great benefit from the administration of the iodids in some form. On the contrary, cautious physicians empirically hesitate to prescribe large doses of the iodids to patients with severe cases of hyperthyroidism for fear of increasing the symptoms. It is a well-known fact that some individuals are very susceptible to the iodids. Berg has reported several cases of patients, receiving full doses of iodids, who rather suddenly developed the symptoms usually noted in hyperthyroidism. Physicians, writing in the early part of the last century, and who, in many things, were very close observers, recognized that there were certain cases of "bronchocele" that were made much worse by large doses of iodids. The following paragraph was written before the time that the train of symptoms known today as hyperthyroidism was generally recognized.

"After a few weeks' skilful administration of potassium iodid the external swelling will gradually disappear. Should the patient, while under a course of it, experience any considerable quickening of the pulse, a rapid loss of flesh, palpitation of the heart, a dry cough, restlessness and want of sleep, and, in certain cases, with an increase of appetite for food, though the swelling shall undergo diminution, it will be necessary to intermit the medicine for some days and afterward resume the use of it when the health and safety of the patient will permit" (Medical Lexicon).

That the thyroid does act as a storehouse to iodin has been demonstrated frequently. It seems possible that it is the iodine, which is not stored or metabolized by the thyroid, which produces the Basedow syndrome. It is more easily stored or metabolized when administered in the pure form than when given in a combined state. The activity of various desiccated thyroid prepara-

tions apparently depends upon their iodine content. Both theoretically and practically they are the most active of the iodine preparations.

On the hypothesis that the symptoms of hyperthyroidism are those produced by chronic iodism, how may the physiology of the thyroid be explained? It is possible that one of the functions of the thyroid is the control iodine metabolism, and that it bears a relation to iodine which might be compared to the relation of the liver with glycogen. There may be conditions under which the thyroid fails in its control of this iodine metabolism, and the continued intake of iodine into the system from natural sources, without its being metabolized, produces the chronic poisoning.

We continually receive from food and water and possibly air a certain amount of iodine in various forms. Seidell and Fenger point out that in cattle, sheep, and hogs there is a seasonal variation in the iodine content of the thyroid glands. Possibly such seasonal variations are from the food which they receive, their iodine content beginning to rise as soon as the pasture comes.

Kocher has shown that patients suffering with Basedow's disease, when treated with iodids, excrete a larger proportion in the urine than do normal individuals. From this it may be inferred that they do not metabolize iodine to the extent the normal person does.

There are many things concerning the toxic goiter which we do not understand, but it may be possible that it is the faulty metabolism by the thyroid as much as the hypersecretion which acts in producing the symptoms known today as hyperthyroidism.

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# A DEMONSTRATION OF A DEPRESSOR SUBSTANCE IN THE SERUM OF THE BLOOD OF PATIENTS AFFECTED WITH EXOPHTHALMIC GOITER\*

J. M. BLACKFORD AND A. H. SANFORD

During the past year we have conducted a series of experiments with a view to throwing further light on the relation of the secretion of the thyroid to exophthalmic goiter. We have studied chiefly the cardiovascular effects on the dog of intravenous injections of sterile non-hemolytic blood-serum from nervous individuals and from patients affected with exophthalmic goiter. Also, numerous saline extracts of goiter have been injected intravenously into dogs and the effects on the blood-pressure studied.

Gley,† in 1911, announced that the serum of certain cases of exophthalmic goiter produces marked cardiac depressor action. He showed, too, that a first injection of potent exophthalmic serum conferred a tolerance of such a nature that subsequent injections of the same serum during the same experiment produced little or no effect.

We have attempted to follow out Gley's researches, injecting intravenously into dogs the serum procured from patients affected with exophthalmic goiter. The effect on blood-pressure was recorded graphically on a long paper kymograph in the usual manner, using the left carotid artery for the arterial cannula. All injections were made into the right femoral vein. The right vagus was ex-

\* Read before the Association of American Physicians, Washington, D. C., May, 1913. Reprinted from the American Journal of Med. Sciences, December, 1913, pp. 796-802. Copyright, 1913, by Lea and Febiger.

† Jour. de Phys. et de Path. Gén., 1911, xiii, 928-941; Cleret: *ibid.*, pp. 955-970.

posed and stimulated by induction shock in certain experiments. Blood was obtained by sterile technic from the median basilic veins of the patients, collected in sterile flasks, and the serum allowed to separate in the cold. The manifest difficulty that must always be encountered in such work, *i. e.*, the impracticability of obtaining a large supply of blood from each case, has somewhat hindered certain experiments, but we believe that our results are sufficiently interesting to justify reporting.

Gley states 5 c.c. of serum per kilo dog weight must be used to obtain the best results. We did not have sufficient serum for such large dosage, but obtained excellent results with smaller doses. We have injected  $2\frac{1}{2}$  to 4 c.c. serum per kilo dog weight as an average dose, and except when stated to the contrary, this has been the amount of serum.

We have used for these experiments the sera from twenty-eight patients having exophthalmic goiter. Other sera examined have included those from normal individuals, from patients having goiters without apparent intoxication, and from patients presenting the picture of a long-standing intoxication, presumably due to adenomas of the thyroid. Only the sera from patients with active symptoms of exophthalmic goiter and with markedly hyperplastic glands, as shown by microscopic examination, have produced in the dogs injected any definite symptoms of cardiovascular depression.

The curves produced by the sera from patients affected with exophthalmic goiter have naturally fallen into three groups:

Group I. Those sera causing more than 30 mm. of Hg drop in blood-pressure.

Group II. Those sera causing a drop in blood-pressure, but less than 30 mm. of Hg.

Group III. Those sera causing no appreciable drop in blood-pressure.

The significance of this classification was observed only after an analysis of the individual cases.

GROUP I.—*Six Sera Causing Drops in Blood-pressure of More than 30 mm. of Hg.*—The four curves in Chart I, all of which

produced drops in blood-pressure of more than 30 mm. of Hg. when injected in doses of 2.5 c.c. per kilo dog weight, were obtained by injecting sera from patients who were at or near the height of an early and severe intoxication, as shown by the following summaries of the case histories:

CASE 69,123.—Female, aged twenty years. Three months before (March, 1912) noticed suddenly all the typical cardiac,

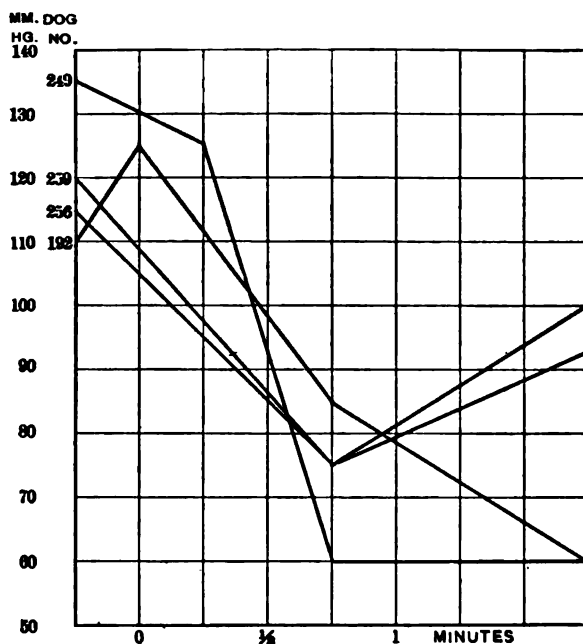


Fig. 238.—Chart 1, drops in blood-pressure of more than 30 mm. after injection of sera from patients in the stage of acute intoxication from exophthalmic goiter.

nervous, and muscular symptoms of Graves' disease. Rapid progress during one month to acute vomiting, with great loss of strength. During the third month vomiting ceased, but all other symptoms were marked. (Experiment conducted on dog 253.)

CASE 69,198.—Female, aged fifty years. Slight goiter noted one year before (May, 1911). Definite typical symptoms of exophthalmic goiter began six months before, with loss of weight, weakness, and nervousness. Two months before violent crisis, with

vomiting, the patient remaining in an acute condition for one week, since then vomiting in spells. In bed most of the time. Loss of thirty pounds in weight in two months. Patient had not noted exophthalmos, which was moderately evident. (Experiment conducted on dog 259.)

CASE 67,993.—Male, aged seventeen years. Three months before (February, 1912) began to lose weight, and all the usual symptoms became evident and rapidly progressed. A month later goiter was noted and the patient forced to bed by weakness. In bed one month, then slight improvement, and has been able to be out of bed the past month, though a marked intoxication is still present. (Experiment conducted on dog 249.)

CASE 68,628.—Female, aged twenty-three years. Six months before (January, 1912) developed nervous and cardiac symptoms and exophthalmos. She rapidly became worse, and at present shows marked intoxication. Diarrhea for one month. Marked loss of strength and fifteen pounds loss of weight. This patient died in an exacerbation following a single ligation. Unfortunately, autopsy on this patient was refused. (Experiment conducted on dog 192.)

We believe these histories show conclusively that the four cases were all acute and severe intoxications. Clinical diagnoses in these as well as the following cases have been confirmed by pathologic examination of the goiters except the one which terminated fatally.

The two cases shown in Chart II are interesting exceptions. One was a fairly acute intoxication of only moderate severity; the other was a chronic intoxication of marked severity. The case histories are as follows:

CASE 75,496.—Male, mulatto, aged thirty years. Past history, gonorrhea, syphilis (positive Wassermann), and some alcoholic excess. Two years before (November, 1910) began to lose weight and strength, and noticed nervous, cardiac, and eye symptoms. Rapid progress to an extreme crisis, with prostration, vomiting, and diarrhea. Then recovery during six months; able to do some work, but still had marked intoxication with a chronic diarrhea. Weight forty pounds below normal. (Experiment conducted on dog 361.)

CASE 69,619.—Female, aged nineteen years. Nine months before (October, 1911) had to stop school on account of weakness, dyspnea, and nervousness. Symptoms progressively worse until forced to bed six months before. After a rest she improved steadily, and presents a clean-cut but not marked picture of exophthalmic goiter. (Experiment conducted on dog 264.)

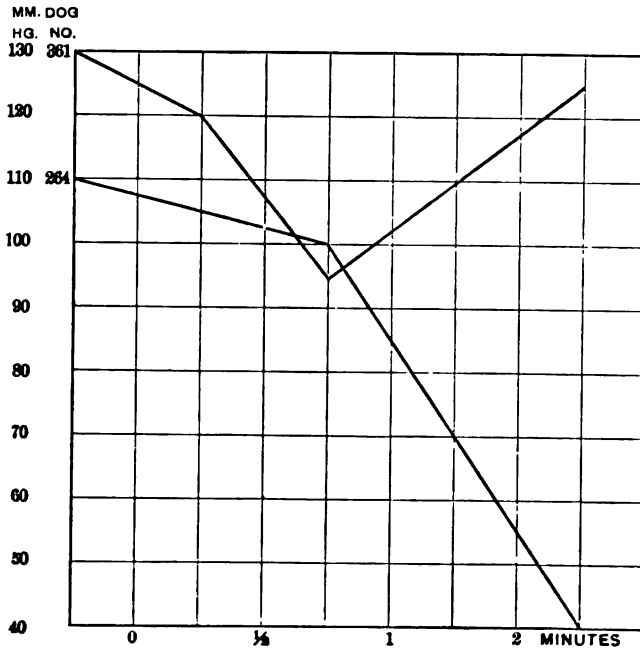


Fig. 240.—Chart 2, drops in blood-pressure of more than 90 mm. after injection of large doses of sera from patients with moderate intoxication from exophthalmic goiter.

From the two preceding histories we may judge that neither case was extreme. On examining our records we find that the doses of serum given each dog were about three times that used to secure the marked effects shown in Chart I. Again, we may note that the first case (75,496) was a chronic and severe one, but gave only a 35 mm. drop in blood-pressure, thus almost admitting it into the next group. The second case (69,619) gave a marked fall in blood-pressure, and though not very severe, was not far past a crisis when the blood was taken.

GROUP II.—*Ten Sera Causing Drops in Blood-pressure of Less than 30 mm. of Hg.*—Chart III shows the curves resulting from injections of six of these sera which cause a fall in blood-pressure of less than 30 mm. of Hg, but which apparently contained a slight amount of the depressor agent. Eight of these ten patients had been afflicted with the disease for more than a year and none of them seemed near any marked exacerbation. In general it may be stated that these cases were of longer standing and with more pronounced intoxication than those in the following group. Two typical histories from this group are as follows:

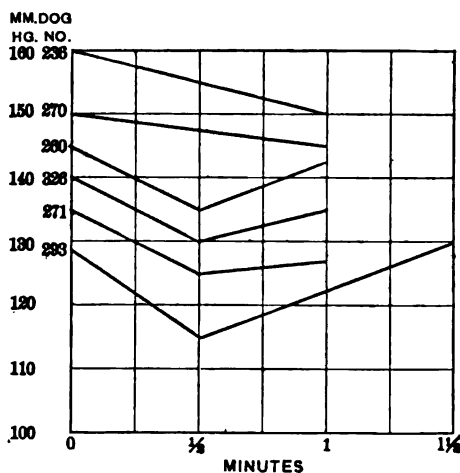


Fig. 241.—Chart 3, drops in blood-pressure of less than 30 mm. after injection of sera from patients not at the height of intoxication from exophthalmic goiter.

CASE 68,883.—Male, aged thirty years. Appendectomy had been done eighteen months before (January, 1910), following which symptoms of exophthalmic goiter promptly appeared and progressed during six months to an extreme intoxication with vomiting, diarrhea, and prostration. Loss of 40 pounds in six months. For the past six months steady improvement, and now is nearly normal in weight, though still affected with definite Graves' disease. (Experiment conducted on dog 253.)

CASE 67,283.—Female, aged thirty-six years. Tremor noted for several years. Always more or less nervous. Increased irri-

tability and gradual loss of strength were noted six months before (November, 1911). No dyspnea. Slight diarrhea during the past month. Working steadily to date. Experiment conducted on dog 236.

**GROUP III.—Thirteen Sera Causing No Appreciable Drop in Blood-pressure.**—Chart IV shows six curves as typical of the 13 inert sera which fall into this group. None of the patients seemed to be near a crisis, and eight of them had been sick less than nine months.

These experiments seem to indicate that patients affected with exophthalmic goiter who are suffering from a marked degree of intoxication at or near the height of the clinical curve of the disease (Plummer) possess serum which has a powerful depressor action. The authors have failed to demonstrate this depressor action by similar means in normal sera, or in sera from patients not having markedly hyperplastic thyroids. Also sera from patients with exophthalmic goiter not at or near the crest of the wave of intoxication are less potent or may be entirely inactive.

Since it was not always thought best to bleed very sick patients, only a small number of experiments have been made with sera from patients with severe intoxications. Yet it may be of interest to know that most of the patients that were bled experienced considerable relief from their subjective symptoms after the bleeding.

The results of intravenous injections into dogs of saline extract of 90 goiters of various kinds from human patients have also

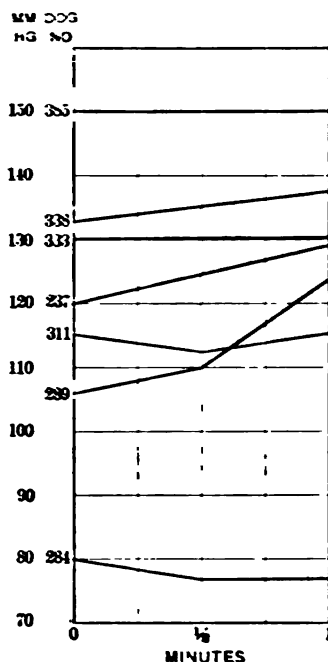


Fig. 242.—Chart 4, no effect on blood-pressure following injection of sera from patients with symptoms of intoxication from exophthalmic goiter, but not at or near crisis.

been made. These experiments may have some bearing on the action of the depressor sera, and a brief report of the results is herewith appended.

*Intravenous Injections of Saline Extracts.*—Experiments with extracts of 48 exophthalmic thyroids have shown that the markedly hyperplastic goiters considered typical of Graves' disease have a more powerful depressor action than that of the extract of any normal organ examined, including muscle, liver, spleen, pancreas, breast, testicle, thyroid, etc. The fall in blood-pressure averages 60 mm. of Hg, and is often considerably more, whereas that from other tissues in any comparable dosage is usually less than 25 mm.

Extracts of adenomas of the thyroid, of simple colloid goiters, and of normal thyroids likewise have a depressor action, which, however, has not been found so marked as that produced by extracts of exophthalmic thyroids. Injections equivalent to as much as 5 gm. per kilo dog weight do not cause a fall as great as that of the extracts of exophthalmic goiters in doses of 0.5 gm. per kilo dog weight.

The first injection of any extract of fresh goiter, as of most extracts of tissue, confers a marked degree of tolerance to subsequent injections of the same material during the same experiment.

As is well known, peptone solutions cause a marked fall in blood-pressure on intravenous injection, and subsequent injections show that a tolerance has been established similar to that produced by extracts from goiters. The depressor action of peptone solution is not, however, affected by a previous dose of the extract of exophthalmic goiter, nor is the action of the extract of exophthalmic goiter affected by a previous dose of peptone solution. On the other hand, it is interesting to note that the depressor action of the extract of an exophthalmic goiter is much diminished by a previous dose of potent serum from a case of toxic exophthalmic goiter, and the reverse, judging from a limited number of experiments, is equally true. In other words, a crossed tolerance seems to exist between the depressor action of extract of exophthalmic goiter and of exophthalmic serum. It seems probable, therefore,



that the depressor agent in the extract of exophthalmic thyroid and that in the serum from a case of exophthalmic goiter are of the same nature.

No attempt has yet been made to identify the chemical nature of the depressor substances in these extracts of thyroids or of those in sera of patients affected with exophthalmic goiter. From certain experimental evidence it seems that the substance is neither cholin nor ordinary peptone.

#### CONCLUSIONS

We believe that the work submitted justifies the following conclusions:

Fresh extracts made from exophthalmic thyroids contain a powerful depressor substance.

A powerful depressor substance likewise exists in the sera obtained from certain cases of exophthalmic goiter.

The latter substance is present in direct proportion to the clinical acuteness and severity of the disease.

The sera from patients with non-hyperplastic thyroids do not have a depressor action.

After an active depressor dose of the serum from a case of exophthalmic goiter the depressor action of the extract of an exophthalmic goiter is weakened or abolished. The converse is also true.

## RESULTS OF INTRAVENOUS INJECTIONS OF EXTRACTS OF GOITER ON BLOOD- PRESSURE IN THE DOG \*

J. M. BLACKFORD AND A. H. SANFORD

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During a rather extensive and still uncompleted study of the effects of intravenous injections of extracts of normal and pathologic organs the authors have made use of many typical exophthalmic and simple goiters. The action of these extracts of goiters has been of interest on account of certain additions to the previous results obtained by Schönborn and Gley, who have performed similar experiments.

Schönborn reports that he was unable to determine any essential difference between the action of intravenous injections of extracts of exophthalmic and simple goiter except that extracts of exophthalmic goiter caused in general a more marked fall in blood-pressure. Gley repeated Schönborn's work, with the same results. Their material was limited, each having but six exophthalmic goiters. Neither author did more than record changes in pulse and blood-pressure, and no records were published showing the mechanism of the fall in blood-pressure. Neither was any record made of the gross or microscopic findings in the glands used.

Much confusion exists regarding the typical gland in exophthalmic goiter. We have used only fresh glands having a parenchymatous hypertrophy and hyperplasia of cuboid to columnar epithelium, and with little or no stainable colloid material (low iodine content). When adenomas occurred in such glands, they were

\* Read before the Association of Pathologists and Bacteriologists, Washington, D. C., May, 1913. Reprinted from the Medical Record, August 30, 1913, pp. 378-380.

dissected out and extracted separately. All goiters, immediately after removal, were macerated with sand for one to three hours in equal weight of normal salt solution. All extracts considered as fresh were injected within five hours of removal and many in less time. Forty-six exophthalmic goiters and nearly as many simple goiters have been thus extracted and injected.

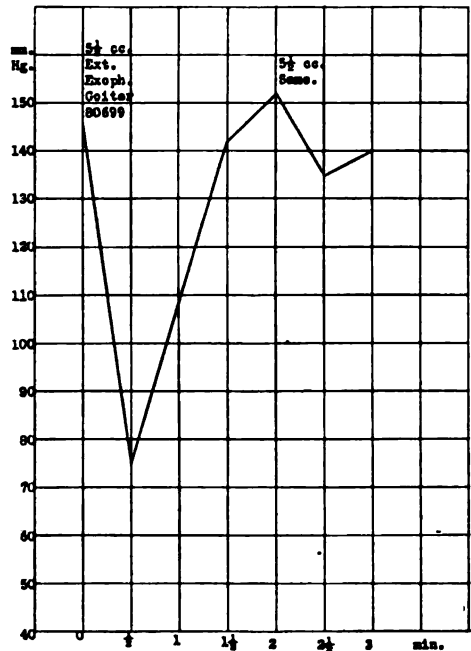


Fig. 243.—Dog 483. Drop due to injection of extract of exophthalmic goiter (hyperplastic thyroid). Dose,  $\frac{1}{2}$  gm. per kilo. Second dose the same. No drop.

The action of extracts of exophthalmic goiters shows itself as follows in dosage equivalent to  $\frac{1}{2}$  gm. goiter per kilo dog weight: From one-quarter to one-half minute following the primary injection there is a sudden fall in blood-pressure, with slowing of the pulse and with diminished amplitude. The extent of the drop averages about 60 mm., a greater drop than that caused by any other extract of organs. The recovery is rapid, as a rule (two to three minutes), though in some instances much slower (fifteen

minutes). A subsequent injection of the same material into the same dog in the same experiment gives little or no effect, provided the extract be fresh. We have made the second injection at intervals varying from two to forty-four minutes after the first injection.

The fall in blood-pressure is accompanied by a marked dilatation of the splanchnic vessels, preceded by a somewhat diminished cardiac output. Respiration is quickened during the vas-

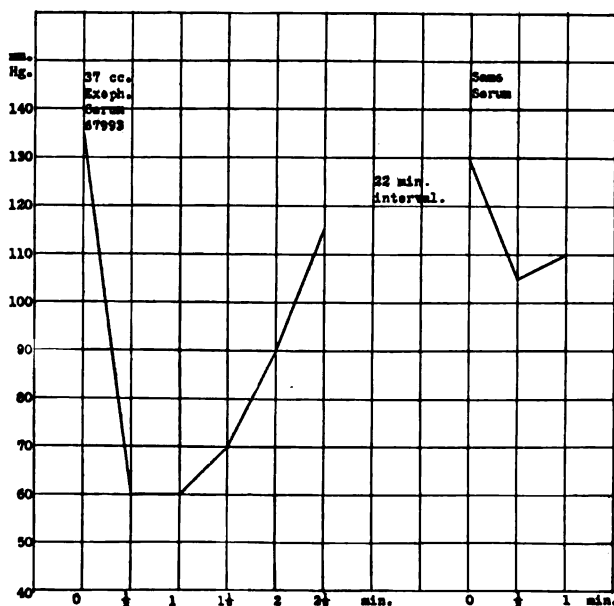


Fig. 244.—Dog 249. Typical drop in blood-pressure due to injection of serum from a patient suffering from the acute intoxication of exophthalmic goiter.

cular change. Atropin blockage of the vagus does not alter the kymographic picture.

In three instances we secured exophthalmic goiters which contained sufficiently large adenomas to permit of separate extraction. With the extracts of the adenomatous portions we obtained tracings similar to those recorded on injections of extracts of simple goiters. The hyperplastic portions yielded extracts containing a much larger amount of depressor substance.

We have classified as simple goiters those glands removed on

account of tumors in the gland (adenomas), and those showing old cystic changes in colloid goiters, sometimes considered as an "adenomatosis." Such extracts in dosage equivalent to  $\frac{1}{2}$  gm. tissue per kilo dog weight gives little effect, and in some instances no demonstrable effect whatever in blood-pressure. By giving a much larger dose,—up to 5 gm. per kilo dog weight,—a more considerable drop in blood-pressure occurs, but we have been unable to obtain any such marked effect even with this high dosage, as on injections of doses of  $\frac{1}{2}$  gm. per kilo dog weight of exophthalmic extracts. We have not observed the "Aktionspulse" of Cyon, described by Schönborn and Gley.

The supposition that the depressor action of the extracts of exophthalmic goiters is a matter of dosage and common to all tissues does not seem to us justifiable. The injection of normal thyroid tissue in much larger dosage gives only a moderate cardiovascular depression, not more than can be obtained by the injection of extracts of most cellular organs in large doses. No extracts of other organs examined give as marked or prolonged a depressor action as the extract of exophthalmic goiters.

These fresh extracts of hyperplastic thyroids are not dependent on cholin for their effect, since atropinization does not alter their action on the blood-pressure. Also heating the extracts to 70° C. in attempts at keeping them has destroyed their depressor action. This would not have occurred had the depressor action been due to cholin.

If the extracts are not fresh (*i. e.*, from eight to twelve hours), the action is different. Atropin lessens or abolishes the depressor action. Also no tolerance to secondary injections is established by the initial dose. Not infrequently a rise instead of a fall in pressure comes with each injection.

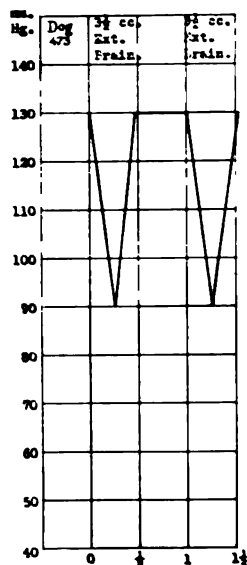


Fig. 245.—Dog 473. Drop in blood-pressure due to injections of extract of brain. Dose,  $\frac{1}{2}$  gm. per kilo. There is no tolerance produced to the second injection typical of cholin.

In conjunction with our experiments on extracts of glands we have injected the sera of patients suffering from exophthalmic goiter at various stages of their intoxication, and as controls have used normal serum and serum from patients having simple goiters. Further details on this phase of our work will be reported elsewhere. Suffice to say that there is a powerful depressor substance demonstrable in the blood of a patient affected with ex-

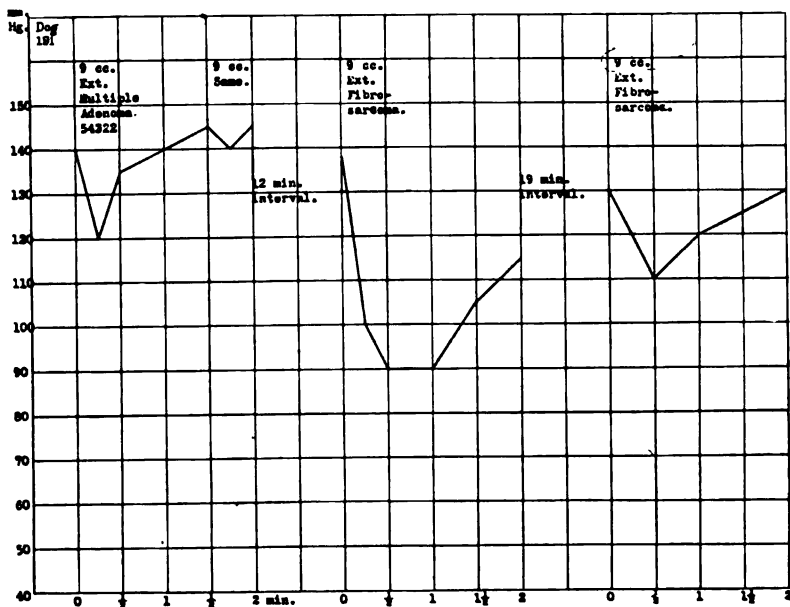


Fig. 246.—Dog 191. First and second injections of extract of multiple adenomas of thyroid, dose  $\frac{1}{2}$  gm. per kilo; 20 mm. drop and tolerance. This was followed by the same sized dose of extract of fibrosarcoma; 48 mm. drop, and tolerance to second injection.

ophthalmic goiter at the height of the intoxication. Moreover, from the crossed tolerance between extracts of hyperplastic thyroids and sera of patients having exophthalmic goiter it would seem that the cardiovascular effect is due to the same depressor substance in each.

The tolerance of a first injection of peptone to subsequent injections of the same depressor does not protect the dog against the action of the extracts of exophthalmic goiters or patients' sera.

In conclusion we may say that—

1. A powerful depressor substance exists in exophthalmic goiters.
2. A primary injection establishes tolerance to the action of further injection.
3. Atropin does not inhibit its action.
4. The substance does not behave physiologically like cholin.

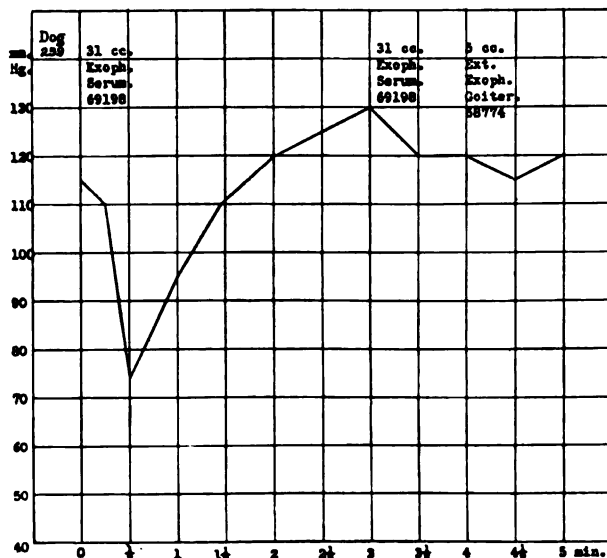


Fig. 247.—Dog 259. Drop of 40 mm. due to injection of serum from patient having exophthalmic goiter. Tolerance to second injection of the same serum and also to a fresh extract of hyperplastic thyroid.

5. The action is chiefly through peripheral dilatation, aided by some diminution in cardiac output.
6. Irritability of the vagus is not decreased.
7. The existence of a crossed tolerance between the depressor action of extracts of exophthalmic goiters and of serum from patients with exophthalmic goiter suggests that the two substances are the same.

#### REFERENCES

- Gley: Jour. de Phys. et de Path. Gén., November 15, 1911, pp. 954-970; and Cleret: *Ibid.*, pp. 928-941.  
 Schönborn: Arch. f. exp. Path. u. Pharmac., 1909, ix, pp. 390-394.

# A COMPARATIVE STUDY OF THE EFFECTS ON BLOOD-PRESSURE OF THE EXTRACTS AND SERA OF EXOPHTHALMIC GOITER AND OF OTHER SUB- STANCES \*

A. H. SANFORD AND J. M. BLACKFORD

When injected intravenously into laboratory animals, extracts of most tissues show the presence of one or more substances, with some depressor action. Rabbits and cats have been used for these experiments, but the dog is the animal best adapted for the purpose. By using an arterial cannula, direct records of blood-pressure are obtained by means of the mercury manometer and the kymograph. It is observed also that with certain substances a marked fall in blood-pressure occurs on the first injection, but on the administration of a second dose a few minutes later a remarkable tolerance is revealed.

The action of peptone on the blood and blood-pressure has been the subject of physiologic investigation for years. This substance causes a marked fall in blood-pressure, with a subsequent tolerance to the same dose when injected intravenously.

Howell, Jordan and Eyster, Dixon and Halliburton, and others, working with pineal extracts, have shown a fall in blood-pressure, followed by a less marked effect on the second injection. A rise in blood-pressure, followed by tolerance, has been shown for the hypophysis by Howell, Lewis, Miller, and Mathews.

\* Read before the Section of Pathology and Physiology, Amer. Med. Assoc., Minneapolis, June 19, 1913. Reprinted from Jour. Amer. Med. Assoc., January 10, 1914, pp. 117-122.



There have been various conflicting results with the intravenous injections of extracts of the thyroid gland. We can confirm the results of Gley, Schönborn, and others that in proper dosage there is a primary fall in blood-pressure and a less marked effect on second injections of extracts of goiters.

Brodie, in his work with horse-serum injected into cats, noted a fall in blood-pressure, with a subsequent tolerance. He noted further that the animal is protected by this first dose against the action of similar substances. He does not state, however, what his control substances were. Gley and Cleret found that in a series of 6 patients suffering from exophthalmic goiter the sera of 2 caused a marked fall in blood-pressure in dogs, and a second dose of the same sera caused little or no effect.

On the other hand, while cholin may cause a marked fall in blood-pressure when injected intravenously, it does not produce a tolerance. Halliburton has shown, by chemical analysis, that cholin is abundant in extracts from brain tissue, and is the depressor substance. This is probably the substance causing lowering in pressure in extracts of any tissue in which proteolytic changes may have occurred. *We believe that if the extract of a tissue shows the presence of a depressor substance without tolerance following, the presence of proteolytic change should be suspected.* It would seem also that this proteolytic change begins in the tissues very soon; thus nothing but fresh extracts should be used.

In our work with the above-mentioned substances and other extracts of tissue we may have gone a step farther than other investigators in that we have used a number of different substances in the same animal. It seems that the action of an extract producing tolerance to subsequent injections is more or less specific. The administration of an extract of another sort of tissue is followed by all the phenomena peculiar to that substance, without regard to that which has been employed previously. This specificity of action is also shown most markedly in the action of peptone, and also in the extracts containing cholin when administered before or after the extracts of tissues. Our protocols (Tables I to X in-

clusive) show the effect produced by these substances on the blood-pressure of the dog.

#### TECHNIC

*Extracts and Solutions.*—All extracts were made from fresh tissue, minced, ground with sand, and mixed with physiologic salt solution, 1 c.c. for each gram of tissue. After macerating for an hour or so the solution was filtered through glass wool. Control extracts from normal dog tissue were made immediately after killing a dog, the brain, thyroid, spleen, pancreas, and testes removed and prepared as above.

It was found that a potent dose of thyroid, especially if the tissue was hyperplastic, was 0.5 c.c. of extract ( $\frac{1}{2}$  gm. of tissue) per kilo. Peptone control was made in 10 per cent. solution and administered in the same dosage—0.5 c.c. per kilo. Various commercial extracts of thyroid were used as controls, and found to possess less marked effect on blood-pressure than fresh extracts.

To obtain serum, the patient was bled into a flask of about 180 c.c. capacity, and on the following day, after contraction of the clot had taken place, the serum was separated. The dose of serum producing marked effect in suitable cases was found to be 2.5 to 4 c.c. per kilo.

*Operative Procedures.*—Dogs anesthetized with ether after a preliminary dose of morphin were used for our series of experiments. For securing a direct blood-pressure tracing on the long paper kymograph the left carotid was used; when the vagus was stimulated, the nerve on the right side was used. The extracts and sera were injected with a suitable sized syringe into the right femoral vein. Half-saturated  $\text{MgSO}_4$  and also the usual  $\text{Na}_2\text{CO}_3$  and  $\text{NaHCO}_3$  solutions were used to prevent clotting. In our first experiments a transmitting tambour was used in producing tracings; later a float and the direct method were employed.

The accompanying tables give a complete record of the experiments performed. Though there are a great many negative results, we feel that they may be of interest to others and that they should be published in detail.

(When a second injection of a substance was made, the record appears immediately below that of the first injection of the same substance)

(When a second injection of a substance was made, the record appears immediately below that of the first injection of the same substance)

### SERIES A.—INJECTIONS OF EXTRACTS OF HYPERPLASTIC THYROIDS FROM EXOPHTHALMIC GOITER PATIENTS

[illegible]

### SERIES B.—INJECTIONS OF EXTRACTS OF HYPERPLASTIC THYROIDS FOLLOWED BY INJECTIONS OF SERA FROM EXOPHTHALMIC GOITER PATIENTS

1	285	7/5/12	7	102	Ext. hyperplast. thy., 3 c.c.	75	27	3	100	Ext. hyperplast. thy., 3 c.c.	90	10	1	92	Exoph. serum, 15 c.c. (Case No. 71058)	85	7	2	110	Peptone (10 per cent.), 10 c.c.	35	75	8
2	274	7/19/12	13	120	Ext. hyperplast. thy., 5.5 c.c. (healed to 60° C.)	60	60	4	90	Ext. hyperplast. thy., 3 c.c.	90	..	5	100	Exoph. serum, 21 c.c.	80	20	5	48	Peptone (10 per cent.), 10 c.c.	45	5	
3	483	5/4/13	11	125	Ext. hyperplast. thy., 5.5 c.c.	125	..	5	135	Exoph. serum, 50 c.c. (Case No. 70483)	135	..	10	140	Ext. hyperplast. thy., 5 c.c.	90	50	..	..	..	..	..	
				130	Ext. hyperplast. thy., 5.5 c.c. (Case No. 80708)	62	68	4	130	Exoph. serum, 28 c.c. (Case No. 86699)	130	10	5	130	Peptone (10 per cent.), 5.5 c.c.	84	46	4	128	Ext. cancerous breast, 5.5 c.c. (Case No. 90779)	106	20	
				128	Ext. hyperplast. thy., 5.5 c.c.	193	..	5	..	..	..	..	..	138	Peptone (10 per cent.), 5.5 c.c.	116	22	4	128	Ext. cancerous breast, 5.5 c.c.	128	..	

SERIES C.—INJECTIONS OF EXTRACTS OF HYPERPLASTIC THYROIDS FOLLOWED BY INJECTIONS OF VARIOUS CONTROL SUBSTANCES

Doc No.	Serial	Date	Weight Kilos	FIRST SUBSTANCE INJECTED			SECOND SUBSTANCE INJECTED			THIRD SUBSTANCE INJECTED			FOURTH SUBSTANCE INJECTED		
				B. P. mm. Hg	Drop mm. Hg	Interval, Mins.	B. P. mm. Hg	Drop mm. Hg	Interval, Mins.	B. P. mm. Hg	Drop mm. Hg	Interval, Mins.	B. P. mm. Hg	Drop mm. Hg	Interval, Mins.
					B. P. $\frac{1}{2}$ Min. Later			B. P. $\frac{1}{2}$ Min. Later			B. P. $\frac{1}{2}$ Min. Later			B. P. $\frac{1}{2}$ Min. Later	
1	229	4/26/12	9.6	131 Ext. hyperplast. thy., 5 c.c. (Case No. 67068)	35 96	40	120 Normal serum, 20 c.c.	123							
2	281	7/5/12	9.5	120 Ext. hyperplast. thy., 5 c.c. 95 Ext. hyperplast. thy., 5 c.c. (heated)	130 95	20 1	95 Iodothyron, 5 c.c. (2 per cent.)	95							
3	248	8/5/12	20.0	95 Ext. hyperplast. thy., 5 c.c. 115 Ext. hyperplast. thy., 10 c.c. Thyroidectomized, June 8th (Case No. 70781)	95 130	2 2	125 Ext. hyperplast. thy., 20 c.c. (Case No. 70871)	120 5	2	120 2 per cent. iodothyron, 5 c.c. 115 5					
4	231	4/20/12	5.4	140 Ext. hyperplast. thy., 5 c.c. (Case No. 67148)	70 70	17	150 Adenoma ext., 2.5 c.c. (Case No. 67148)	145 5		115 2 per cent. iodothyron, 10 c.c. 125					
5	169	5/3/12	15.6	139 Ext. hyperplast. thy. (Case No. 67250)	100 39	8	125 Colloid adenoma, 20 c.c. (Case No. 32031)	125	4	125 Normal dog thyroid, 20 c.c. 127					
6	239	5/9/12	12.65	140 Ext. hyperplast. thy., 4 c.c. (Case No. 58335)	115 25	2	140 Colloid adenoma ext., 7 c.c. (Case No. 67479)	140	3	145 Cystic adenoma ext., 25 c.c. (Case No. 67503)	150	1	140 Prostate ext., 25 c.c. (Case No. 67251)	130 10	
7	246	5/17/12	22.5	135 Ext. hyperplast. thy., 11 c.c. (Case No. 67104)	75 60	14	135 Ext. colloid adenoma, 11 c.c. (Case No. 67857)	135	13	145 Ext. hyperplast. thy., 11 c.c. (Case No. 67164)	140 5				
8	468	2/17/13	4.5	128 Ext. hyperplast. thy., 2.5 c.c. 110 Ext. hyperplast. thy., 2.5 c.c. 170 Ext. hyperplast. thy., 2.5 c.c.	65 63 86 34	1 125 5	110 Ext. brain, 5 c.c. 98 Ext. pituitary gland, 1 c.c. (heated)	60 50 70 55 87 92	2 16						
9	378	11/26/12	4.6	140 Ext. hyperplast. thy., 2.3 c.c. (Case No. 73935)	102 38	5	110 Ext. pituitary gland, 1 c.c. 160 Peptone (10 per cent.), 2 c.c. (Case No. 72501)	110 rise 81 69	5	140 Exoph. serum, 5 c.c. (Case No. 72498)	130 10				
10	360	11/7/12	4.4	155 Ext. hyperplast. thy., 2 c.c. (Case No. 72501)	69 86	5	160 Peptone (10 per cent.), 2 c.c. 140 Peptone (10 per cent.), 2 c.c. (Case No. 80293)	81 25 115 25	5	150 Peptone (10 per cent.), 2.5 c.c. (Case No. 69547)	70 60				
11	478	2/21/13	5.0	142 Ext. hyperplast. thy., 2.5 c.c. (Case No. 75405)	70 72	6	135 Ext. cancerous breast, 5 c.c. 145 Ext. cancerous breast, 5 c.c. (heated)	120 35 110 35	5	95 Peptone (10 per cent.), 2.5 c.c. 105 Peptone (10 per cent.), 2 c.c. (Case No. 59547)	80 35 105 5		(0.4 c.c. adrenalin administered.)	130 Peptone (10 per cent.), 10 c.c.	Dog kept
12a	283	7/12/12	12.0	156 Ext. hyperplast. thy., 2.5 c.c. 105 Ext. hyperplast. thy., 4 c.c. (heated)	150 6 105	1	105 Ext. hyperplast. thy., 4 c.c. (heated)	105 105	5						
12b	283	7/19/12	12.0	105 Ext. hyperplast. thy., 4 c.c. 135 Peptone (10 per cent.), 10 c.c. 160 Peptone (10 per cent.), 10 c.c.	105 55 145	3 2									

SERIES D.—INJECTIONS OF SERA FROM EXOPHTHALMIC GOITER PATIENTS

1	192	6/6/12	9.5	125 Exoph. serum, 21 c.c. (Case No. 68628)	50 75	9
2	262	6/24/12	6.6	100 Exoph. serum, 21 c.c. 125 Exoph. serum, 21 c.c. (Case No. 69547)	80 20 115 10	
3	353	9/7/12	9.0	130 Exoph. serum, 30 c.c. (Case No. 59547)	130	
4	457	2/8/13	11.0	95 Exoph. serum.		Dog died at once. Injection into external jugular

**SERIES E.—INJECTIONS OF SERA FROM EXOPHTHALMIC GOITER PATIENTS FOLLOWED BY INJECTIONS OF EXTRACTS OF HYPERPLASTIC THYROIDS**

Doc No.	Serial	Kennel	DATE	WEIGHT KILOGS	FIRST SUBSTANCE INJECTED				SECOND SUBSTANCE INJECTED				THIRD SUBSTANCE INJECTED				FOURTH SUBSTANCE INJECTED						
					B. P.	MM. Hg	DROP MM. Hg	B. P. ½ MIN. LATER	INTERVAL, MINS.	B. P.	MM. Hg	DROP MM. Hg	B. P. ½ MIN. LATER	INTERVAL, MINS.	B. P.	MM. Hg	DROP MM. Hg	B. P. ½ MIN. LATER	INTERVAL, MINS.	B. P.	MM. Hg	DROP MM. Hg	
1	259		6/19/12	9.8	110	Exoph. serum, 31 c.c. (Case No. 69198)	75 35	5	120	Ext. hyperplast. thy., 5 c.c.	115	5	3	115	Ext. hyperplast. thy., 5 c.c. (decomposed).	70 45	3						
2	361		11/1/12	7.0	130 129	Exoph. serum, 31 c.c. Exoph. serum, 8 c.c. (Case No. 75496)	95 10 95 34	5	115 150	Ext. hyperplast. thy., 10 c.c. Ext. hyperplast. thy., 3.5 c.c. (Case No. 69368)	110 140	5 10	4 13	100	Ext. hyperplast. thy., 5 c.c.	70 30							
3	381		12/3/12	7.5	160	Exoph. serum, 30 c.c.	135 25	3	165	Ext. hyperplast. thy., 10.5 c.c. (Case No. 69368)	98	22	2	140	Peptone (10 per cent.), 3 c.c.	100 40	3						
4	342		9/21/12	5.5	164	Exoph. serum, 4 c.c. (Case No. 75389)	145 21	7	132	Ext. hyperplast. thy., 4 c.c. (Case No. 73551)	132	13	8	130	Peptone (10 per cent.), 3 c.c.	115 15					152	Ext. hyperplast. thy., 3 c.c. (eight days old)	94 mm. rise
5	270		7/9/12	7.2	150	Exoph. serum, 25 c.c. (Case No. 70119)	135 15	5	150	Ext. hyperplast. thy., 3.5 c.c.	135	15	4	130	Ext. hyperplast. thy., 3 c.c.	115 10					155	Ext. hyperplast. thy., 3 c.c.	35 mm. rise
6	396		9/13/12	10.0	150 140	Exoph. serum, 25 c.c. Exoph. serum, 21 c.c.	130 10	2	140	Ext. hyperplast. thy., 4 c.c. (Case No. 73551)	126	6	2	130	Ext. hyperplast. thy., 3 c.c.	122					122	Ext. hyperplast. thy., 3 c.c.	190
7	338		9/18/12	7.3	120	Exoph. serum, 21 c.c. (Case No. 73673)	125 ..	5	155	Ext. hyperplast. thy., 3.5 c.c. (Eight hours old)	100	55	2	120	Ext. hyperplast. thy., 9 c.c. (eight hours old)	75 45							
8	284		7/12/12	7.0	80	Exoph. serum, 45 c.c. (Case No. 71431)	75 5	2	85	Ext. hyperplast. thy., 3.5 c.c. (heated) (Case No. 70927)	80	30	2	85	Ext. hyperplast. thy., 7 c.c. (heated) (Case No. 71425)	85 50					85	Peptone (10 per cent.), 10 c.c.	50
9	311		9/4/12	7.6	115	Exoph. serum, 30 c.c.	113 2	1	100	Ext. hyperplast. thy., 7 c.c. (heated) (Case No. 73096)	85	15	2	105	Ext. hyperplast. thy., 5 c.c. (decomposed)	85 ..					62	Peptone (10 per cent.), 10 c.c.	17
10	385		12/11/12	12.0	118 150	Exoph. serum, 30 c.c. Exoph. serum, 50 c.c. (Case No. 76590)	117 1 150 ..	5 1	100 150	Ext. hyperplast. thy., 12 c.c. Ext. hyperplast. thy., 6 c.c. (Case No. 76597). After ab grain atropin.	100 108	42	2	105	Ext. hyperplast. thy., 5 c.c.	75 30							
					130	Ext. hyperplast. thy., 12 c.c.	72 58																

SERIES F.—INJECTIONS OF SERA FROM EXOPHTHALMIC GOITER PATIENTS FOLLOWED BY INJECTIONS OF VARIOUS CONTROL SUBSTANCES

Doc No.	Serial	Kennel	DATE	WEIGHT KILOGS	FIRST SUBSTANCE INJECTED				SECOND SUBSTANCE INJECTED				THIRD SUBSTANCE INJECTED				FOURTH SUBSTANCE INJECTED			
					B. P.	MM. Hg	INTERVAL, MINS.	DROP MM. Hg	B. P.	MM. Hg	INTERVAL, MINS.	DROP MM. Hg	B. P.	MM. Hg	INTERVAL, MINS.	DROP MM. Hg	B. P.	MM. Hg	INTERVAL, MINS.	DROP MM. Hg
1	236		5/14/12	12.7	160			140 20	5	160	Fluid cystic adenoma, 5 c.c. (Case No. 67217)	150 10	12	140	Ext. adenoma, 4 c.c. (Case No. 59331)	140				
2	249		5/20/12	9.52	135			60 75	26	130	Ext. prostate, 5 c.c. (Case No. 67221)	70 60	14	130	Ext. multiple adenomas, 12 c.c.	90 30				
3	253		6/9/12	12.5	145			105 35	13	105	Exoph. serum, 20 c.c. (Case No. 68720)	135	3	130	Ext. multiple adenoma, 12 c.c.	115 5				
								115 30	3	135	Exoph. serum, 20 c.c. (Case No. 68893)	135	3	130	Ext. colloid adenoma (Case No. 68352)	115 5	2	110	Ext. colloid adenoma, 7 c.c. (Case No. 68572)	120 10
4	264		6/25/12	5.8	110			125 10	5	105	Ext. multiple adenomas, 3 c.c.	105	1							
								40 70	12	105	Ext. multiple adenomas, 5.5 c.c.	100 5								
5	280		6/21/12	8.2	145			135 10	1	145	Exoph. serum, 21 c.c. (Case No. 69364)	135 10	1	150	Ext. colloid adenoma, 7 c.c.	105 45	3	135	Ext. hyperplast. thy., 2.5 c.c. (Case No. 69116)	120 15
6	271		7/2/12	9.0	135			135 10	10	135	Ext. toxic adenoma serum, 12 c.c. (Case No. 69752)	135	7	130	Ext. hyperplast. thy., 4.5 c.c.	115 5				
7	237		5/1/12	15.0	120			125 5	5	130	Ext. prostate, 6 c.c. (Case No. 66158)	65 75								
8	289		8/19/12	5.0	105			110	3	95	Peptone (10 per cent.), 5 c.c.	55 40	5	105	Ext. hyperplast. thy., 2.5 c.c. (heated) (Case No. 67913)	95 10	2			
					110			100 10	2	110	Peptone (10 per cent.), 5 c.c.	95 15	5	95	Ext. hyperplast. thy., 2.5 c.c.	105				
9	479		2/21/13	5.0	100			90 10	30	120	Ext. cancerous breast, 5 c.c.	105 15	1							
										130	Ext. cancerous breast, 5 c.c.	120	2	140	Peptone (10 per cent.), 5 c.c.	70 70	3	150	Ext. hyperplast. thy., 3 c.c. (two days old)	146 4
10	484		2/26/13	7.0	140			110 30	5	130	Right vagus blocked			142	Peptone (10 per cent.), 5 c.c.	136 6	5			



**SERIES J.—INJECTIONS OF VARIOUS CONTROL SUBSTANCES**

Dog No.	Kennel	Date	Weight Kilos	FIRST SUBSTANCE INJECTED			SECOND SUBSTANCE INJECTED			THIRD SUBSTANCE INJECTED			FOURTH SUBSTANCE INJECTED														
Serial				B. P. mm. Hg	Interval, Mins.	B. P. $\frac{1}{2}$ Min. Later	Drop mm. Hg	B. P. mm. Hg	Interval, Mins.	B. P. mm. Hg	Interval, Mins.	B. P. $\frac{1}{2}$ Min. Later	Drop mm. Hg	B. P. mm. Hg	Interval, Mins.	B. P. $\frac{1}{2}$ Min. Later	Drop mm. Hg										
1	154	5/24/12	20.0	135	2	135	Ext. ovarian, 5 c.c. (Case No. 67988)	115	10	125	Ext. myoma uterus, 30 c.c. (Case No. 67988)	120	5	1	130	Ext. multiple adenoma, 10 c.c. (Case No. 67963)	120	10									
2	224	4/21/12	8.9	140	Autopsy serum, 35 c.c. (Case No. 66323)	80	60	..	..	..	..	..	..	..	..	..	..										
3	227	4/22/12	9.0	130	Normal horse serum, 20 c.c.	148	..	140	Autopsy exoph. serum, 40 c.c. (Case No. 66323)	90	30	..	..	..	..	..	..										
4	235	4/30/12	14.5	147	Autopsy serum, 20 c.c. (Case No. 66649)	95	52	6	110	Ext. adenoma, 7 c.c. (Case No. 48778)	90	20	8	110	Ext. adenoma (Case No. 67017)	97	13	8	90	Ext. hyperplast. thy., 6 c.c. (Case No. 67047)	40	50					
5	228	5/1/12	11.0	140	Autopsy serum, 20 c.c. (Case No. 66649)	95	45	20	115	Ext. multiple adenoma, 7 c.c. (Case No. 66993)	110	3	..	115	Ext. deg. coll. adn., 7 c.c. (Case No. 67056)	95	30	130	Ext. hyperplast. thy. (twenty-four hours old)	60	70						
6	275	7/12/12	12.0	125	Serum (normal?), 50 c.c. (Case No. 70302)	95	30	..	..	110	Ext. multiple adenoma, 7 c.c.	111	..	12	115	Ext. deg. coll. adn., 5 c.c.	110	5	21	..	..	..					
7	244	5/13/12	13.3	140	Ext. dog goiter, 6 c.c. (No. 245)	90	50	..	..	130	Ext. multiple adenoma, 3 c.c.	130	..	..	..	..	..	..	..	..	..	..					
8	241	5/11/12	8.65	135	Ext. dog goiter, 2 c.c. (No. 245)	130	15	1	110	Ext. colloid adenoma, 25 c.c. (Case No. 66476)	90	20	..	..	..	..	..	..	..	..	..	..					
9	471	2/8/13	6.0	115	Ext. dog goiter, 4.5 c.c. (No. 245)	90	25	10	118	Ext. hyperplast. thy., 3 c.c.	102	16	Clot	6	106	Ext. hyperplast. thy., 3 c.c. (decomposed?)	88	18	1	106	Ext. brain, 3 c.c.	65	41				
10	467	2/17/13	6.0	120	Ext. dog thyroid, 3 c.c.	110	..	2	112	Ext. hyperplast. thy., 3 c.c.	112	..	3	130	Ext. hyperplast. thy., 3 c.c.	75	45	1	130	Ext. normal spleen, 3 c.c.	120	..	90	30	1		
11	298	8/20/12	7.8	126	Ext. dog thyroid, 3 c.c.	110	16	1	124	Ext. hyperplast. thy., 3 c.c.	110	14	1	130	Ext. normal spleen, 3 c.c.	120	..	3	130	Ext. normal brain, 3 c.c.	125	..	114	11			
12	475	2/17/13	7.0	125	Peptone (10 per cent.), 4 c.c.	100	65	3	115	Ext. hyperplast. thy., 3 c.c.	115	3	7	130	Ext. hyperplast. thy., 3 c.c.	60	55	7	130	Ext. normal spleen, 3 c.c.	125	..	114	11			
13	474	2/19/13	6.0	122	Peptone (10 per cent.), 3 c.c.	117	5	5	130	Peptone (10 per cent.), 12 c.c.	100	27	2	130	Ext. brain, 3.5 c.c.	90	40	1	130	Ext. brain, 3.5 c.c.	90	40	1	130	Ext. spleen, 3 c.c.	90	18
				100	Peptone (10 per cent.), 3 c.c.	122	48	2	110	Ext. normal thy., 6 c.c.	103	25	3	108	Ext. testis, 3 c.c.	93	13	3	108	Ext. testis, 3 c.c.	108	2	2	112	Ext. spleen, 3 c.c.	106	6



SERIES 7.—INJECTIONS OF VARIOUS CONTROL SUBSTANCES (Continued)

Serial	Doo No.	Kennel	DATE	WEIGHT KILOGS	FIRST SUBSTANCE INJECTED				SECOND SUBSTANCE INJECTED				THIRD SUBSTANCE INJECTED				FOURTH SUBSTANCE INJECTED			
					B. P. MM. Hg	INTERVAL, MIN.	DROP MM. Hg	B. P. ½ MIN. LATER	B. P. MM. Hg	INTERVAL, MIN.	DROP MM. Hg	B. P. ½ MIN. LATER	B. P. MM. Hg	INTERVAL, MIN.	DROP MM. Hg	B. P. ½ MIN. LATER	B. P. MM. Hg	INTERVAL, MIN.	DROP MM. Hg	B. P. ½ MIN. LATER
14	472		2/18/13	5.5	155	Ext. spleen, 2.5 c.c.	125 30	80	145	Ext. brain, 2.5 c.c.	65	1	150	Ext. hyperplast. thy., 2.5 c.c. (Case No. 78665), Decomposed	132 18	1				
15	392		12/21/12	5.8	150	Ext. spleen, 2.5 c.c.	135 15	98	135	Ext. brain, 2.5 c.c.	37	5	145	Ext. hyperplast. thy., 2.5 c.c.	118 27	3	146	Ext. normal brain, 3 c.c.	88	58
					146	Ext. normal spleen, 3 c.c.	180 20	130	138	Ext. normal pancreas, 3 c.c.	28	2	160	Ext. normal thy., 3 c.c.	150 10	3				
					134	Ext. normal spleen, 3 c.c.	171 18	10	160	Ext. pancreas, 3 c.c.	35	9	138	Ext. brain, 3 c.c.	80 58		153	Ext. normal brain, 3 c.c.	112	41
16	382		12/21/12	5.8	145	Ext. spleen, 3 c.c.	118 40	125	160	Ext. pancreas, 3 c.c.	35	9	138	Ext. brain, 3 c.c.	80 58					
					145	Ext. spleen, 3 c.c.	170 (preliminary rise)						160	Ext. brain, 3 c.c.	108 52					
					142	Ext. normal pancreas, 4 c.c.	142 13	135	155	Ext. normal liver, 4 c.c.	20	1	163	Ext. normal prostate, 4 c.c.	143 20	1	170	Ext. normal spleen, 4 c.c.	190	53
17	391		12/21/12	8.2	142	Ext. normal pancreas, 4 c.c.	125 17	138	148	Ext. normal liver, 4 c.c.	10	2	168	Ext. normal prostate, 4 c.c.	164 4	1	170	Ext. normal spleen, 4 c.c.	117	100
18	168		5/4/12	17.0	157	Ext. myoma uterus, 20 c.c.	165	70	155	Ext. fetal adenoma, 50 c.c. (Case No. 67344)	85	17	140	Ext. normal dog thy., 10 c.c.	140				154	16
19	240		5/8/12	12.6	125	Ext. normal muscle, 15 c.c.	190 5	118	125	Ext. chronic mastitis, 13 c.c. (Case No. 57176)	7	2	120	Ext. colloid adenoma, 13 c.c. (Case No. 51564)	125	2	115	Ext. prostate, 17 c.c. (Case No. 65652)	80	55
20	250		5/29/12	16.2	140	Ext. normal muscle, 8 c.c.	135 5	180	140	Normal salt, 16 c.c.	10	2	140	Ext. multiple adenoma, 8 c.c. (Case No. 68166)	135 5	3				
21	288		8/21/12	7.0	140	Ext. normal muscle, 16 c.c.	190 20	115	135	Peptone (10 per cent.), 5 c.c.	20	1	125	Ext. multiple adenoma, 8 c.c. (Case No. 78078)	140		120	Ext. simple goiter, 10 c.c. (Case No. 71566)	130	
					145	Iodothylin, 2 per cent., 10 c.c.	146	125	130	Peptone (10 per cent.), 5 c.c.	5	5								

## DISCUSSION OF TABLE

The first experiment tabulated in Series A shows the great drop in blood-pressure produced by a single injection of extract of hyperplastic thyroid. A 2 demonstrates the presence of an unusually potent depressor, as is also shown by the effect of the same extract in E 6. The tolerance produced by the first injection toward subsequent injections is shown in A 3. In general it may be stated that this tolerance is most manifest when the first injection produces a marked reaction. A 5 shows good tolerance to fresh extracts after the first injection, and also the typical action on both first and second injections of decomposed extracts. Atropin inhibits the action of cholin; that this drug has no effect on the action of the depressor in fresh extracts of hyperplastic thyroids is shown in experiment A 6.

Series B is small, but at least two of the experiments are of interest. The same phenomenon may be noted in both B 2 and B 3, that is, tolerance produced by a good drop on the first injection of extracts of hyperplastic thyroid, and the lack of any effect when serum from a patient having exophthalmic goiter is injected. The second extract injected in B 2 probably had undergone some proteolytic change. B 3 also shows the action of a peptone solution and extract of carcinoma, with tolerance to second injections of each substance.

Four experiments in Series C 4, 5, 6, and 7 show no effect when extracts of non-hyperplastic goiters were injected after primary injections of extracts of goiters with hyperplasia. Iodothyryn was used twice in this series (C 2 and C 3) as a control substance, with no effect. C 8 illustrates well the action of extract of brain. This is probably a cholin action; the comparison between this action and that of decomposed extracts is striking. (See A 5.) The tolerance toward the pressor substance on second injections of pituitary extract shown in C 9 is characteristic of this extract.

The effects of injecting sera from patients with different degrees of intoxication have been made the subject of a separate study and are reported elsewhere. The patients from whom

serum was used in Series D 1, E 1, E 2, F 2, F 4 were all acutely toxic from exophthalmic goiter. The rest were not at or near the height of their intoxication. The apparent tolerance for extracts of hyperplastic goiters by first injecting serum from patients having exophthalmic goiter is seen in E 1, E 2, and E 4. We would expect greater drops in blood-pressure here, as the extracts were made from typical hyperplastic goiters. D 4 also is worthy of note as concerns the last substance used. This extract, eight days old, gave a remarkable rise in blood-pressure each time it was injected. It is evident in E 7 that eight hours is sufficient time in which to produce marked change in the character of an extract.

Series F requires but little comment. The great effect of injecting serum in F 2 had no effect on the subsequent action of an extract of prostate. F 7 also shows the marked depressor action of extracts of this last-mentioned tissue. Atropin has no effect on the action of peptone (F 10), but does inhibit the action of a decomposed extract in the same experiment.

The six experiments in Series G show, on first injection, the presence of a depressor substance, in non-hyperplastic goiters (adenomas) somewhat similar in action to that of extracts of goiters with hyperplasia. That there is at least great difference in dosage is brought out in G 4, where there was a fall of 30 mm. on injecting an extract of hyperplastic goiter after tolerance was established to extracts of adenomas. The action of extract of sarcoma after extract of goiter (G 5) should be noted, and that of extract of carcinoma of the breast after cutting both vagi (G 2).

Of Series H, very little is to be said regarding the three experiments in which serum from patients with simple, non-hyperplastic goiter was injected first. The second experiment in this series shows the more marked effect of serum from patients having exophthalmic goiter, also an apparent tolerance produced thereby for extract of hyperplastic goiter. The cause of death in H 3 is unexplained.

The experiments in Series I add little to our knowledge. However, the marked action of the extracts of exophthalmic goiter is emphasized in comparison with the control substances in the first

three experiments, and I 4 is of interest because of the action of the serum after the large drop and tolerance from extract of sarcoma.

Series J, the last large group of experiments, shows the action of various control substances. J 7, 8, 9, and 10 have been grouped together, because extracts of thyroids from dogs were injected. The results were not constant, however. Peptone was the only substance used in J 11. Tolerance was established to the first dose. When three times this amount was administered, there was a large drop, with tolerance to another injection of the same quantity. The strange preliminary rise of the blood-pressure, followed by a fall, caused by extracts of spleen, occurred in only the three experiments, J 15, J 16, and J 17.

While a study of the individual experiments shows many exceptions, our general findings are stated in the summary.

#### SUMMARY

1. Extracts of exophthalmic goiters cause a very marked fall in the blood-pressure of the dog, with splanchnic dilatation and slowing of the pulse. The first injection produces tolerance toward subsequent injections. Atropin does not affect the action.

2. The serum of patients at the height of intoxication from acute exophthalmic goiter causes a marked fall in blood-pressure; tolerance is produced.

3. The only substances we have used that produce comparable drops in blood-pressure with tolerance are Witte's peptone (10 per cent. solution), extracts of sarcoma, and hypertrophied prostates.

4. Brain extracts and extracts of decomposing tissue containing cholin produce very different drops in that there is no tolerance produced and atropin inhibits their action.

5. The tolerance produced to extracts of sarcoma, prostate, or peptone solutions does not protect the animal from the typical action of the extracts of exophthalmic goiter.

6. The tolerance of the serum of exophthalmic goiter apparently

protects the animal against the action of the extracts of exophthalmic goiter.

In conclusion we would state: There is a powerful depressor substance in saline extracts of exophthalmic goiters, and apparently the same substance is present in the blood of individuals suffering acutely from this disease.

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## GOITER: THE RELATION OF ITS SYMPTOMS AND PATHOLOGY \*

CHARLES H. MAYO

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Certain physiologic facts concerning the thyroid are definitely known, though its exact function is still an unsettled question. Absence of the thyroid in young animals, either natural or experimental, markedly retards their mental and physical development and inhibits the maturity of sex. Total removal of the gland in the adult animal causes mental and physical deterioration, resulting in a condition parallel to that known in man as myxedema, a symptom-complex due to thyreopriva. Experimental hyperthyroidism has not proved successful, though certain symptoms of toxemia are easily induced by feeding thyroid.

It has been shown that the thyroid contains a considerable amount of iodine in organic combinations, the amount varying in inverse ratio to the amount of hyperplasia in the gland. Iodine medication speedily increases the iodine content of the gland, and usually reduces, though it may increase, its size.

The gland is physiologically susceptible to various influences. The internal secretions of the thyroid, the pancreas, and some of the other organs of the chromaffin system represent a series of interacting inhibitory and excitatory influences.

Plummer has called attention to the fact that clinically there are two distinct groups of toxic goiters, one exophthalmic and the other toxic, but non-exophthalmic. Exophthalmic goiter is a definite clinical complex always associated with hyperplasia of the thyroid, and should be sharply distinguished from the con-

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stitutional state or states that may develop with non-hyperplastic goiter. Plummer states: "The onset of exophthalmic goiter is, as a rule, relatively acute, and the course of the disease fairly definite. The clinical picture early in the history is that of a toxin acting directly on the more vital organs, more notably the central nervous and vascular system. Later it is made more complex by the interaction of those organs whose functions have been directly disturbed by the toxin. The order of onset of the more important symptoms based on the average of a series of cases is as follows: (1) Cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of weight; (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice, and (13) death."

Wilson shows that not only is there a constant association of primary parenchymatous hypertrophy and hyperplasia of the thyroid with exophthalmic goiter, but that, further, both the clinical stage and the clinical severity of the disease may be estimated from the stage and severity of the pathologic changes.

He shows further that toxic non-exophthalmic goiters and atoxic simple goiters (following Plummer's classification) do not show pathologically primary parenchymatous hypertrophy and hyperplasia, but that the pathology of the thyroid in these cases is a regeneration of a previous atrophic parenchyma, a development of encapsulated adenomas (of either fetal or adult type of parenchyma), or, as is most usual in atoxic simple goiter, an enlargement of the gland through distention of its alveoli by retained colloid secretion accompanied by a thinning and atrophy of the parenchyma.

While various toxins may cause degeneration of the essential organs, for example, heart, liver, kidneys, etc., the toxin causing the symptom-complex which we designate "thyrotoxicosis" must be associated with definite pathologic changes in the thyroid, that is, hypertrophy, hyperplasia, etc., in order to prove its origin therein.

Some cases of mild exophthalmic goiter recover spontaneously;

others yield to careful hygienic treatment, which consists essentially of rest, quiet, mild exercise in the open air, reduced nitrogenous diet, etc. Specific medication has been largely based on the assumption that the symptoms are due to the absorption of a toxin from the gland, and efforts have been made to neutralize the toxin or to immunize the patient against its effect.

The administration of iodine, both internally and externally, is one of the oldest forms of medical treatment for goiter, but even now, after the enormous amount of study which has been made of the relationship of the iodine content of the thyroid in relation to the symptoms of Graves' disease by Baumann, Marine, Hunt, Smith, and others, the administration of the drug is still far from being on a scientific basis.

In relation to the surgical treatment of exophthalmic goiter of severe intoxication, it must be constantly borne in mind that we are dealing with a chronic condition regularly presenting improvement, followed by exacerbation of symptoms. In the severe cases growing worse operation must not be performed. These cases are for a time medical, and emergent surgery is not indicated.

As a preparation for thyroidectomy in severe cases of hyperthyroidism rest treatment to quiet the heart improves active symptoms; the use of the Roentgen-ray will sometimes cause temporary amelioration of the more severe symptoms, and in the still more serious cases of this type the injection of 1, 2, or 3 drams of boiling water (Porter's method) into a lobe of the gland acts favorably in improving the condition of the patient.

Our own experience in the ligation of vessels for the relief of exophthalmic goiter covers a period of more than twenty years, and from results obtained it seems indicated that the vessels, and at times a portion of the gland, should be ligated in certain cases. First, in those patients suffering from mild symptoms of hyperthyroidism which are hardly severe enough to warrant a thyroidectomy; second, in that large group having acute, severe exophthalmic goiters, and the chronic and very sick patients who, having exhausted all forms of treatment, are now suffering from various secondary symptoms; and, third, in cases of marked pulsation



and thrill of the thyroid arteries, associated with dilatation of the heart and loss of weight. Great improvement follows the ligation in these cases and later thyroidectomy is advised, since there may be a relapse to the former condition. Should the condition recur before a partial thyroidectomy is made, or should a severe relapse occur after partial extirpation, the inferior thyroid artery should be ligated and half the remaining lobe removed when improvement occurs.

To prevent the possibility of tetany in operating on the thyroid, the parathyroid glands must be avoided and preserved even if it be necessary to replace accidentally separated ones beneath the capsule of the thyroid at the pole of the gland. Such areas must be free from bleeding to insure growth of the graft. These bodies are known to be occasionally injured by hemorrhages into them at birth, so it is impossible to determine whether or not they are all present, and whether or not the one or two that may be injured in the course of the operation are the only ones existing.

In the early development of surgery operations on exophthalmic goiters were delayed until serious complications arose with the heart, kidneys, nervous system, etc., which led to a high mortality—an average of 25 per cent. in the advanced cases. The present mortality varies from 1 to 3 per cent. The various causes of mortality are acute hyperthyroidism, embolism, pneumonia, hemorrhage, sepsis, etc.

The toxic non-exophthalmic goiters are divided by Plummer into two merging groups: (1) A group in which the cardiac toxin predominates, and the clinical picture closely resembles and in many instances cannot be differentiated from the cardiovascular complex resulting from alcoholic, luetic, septic, and other well-known toxins; (2) a group more closely approaching the picture of Graves' disease, and including the cases that have been erroneously so diagnosed by the mass of the profession.

The treatment of toxic non-exophthalmic goiter is, in the mild or early stages (Plummer's group 1), practically the same as that of simple goiter. In its severe or advanced stages (Plummer's

group 2) the mortality is as high as, or higher than, that of exophthalmic goiter of similar severity and stage of symptoms.

Until Plummer's differentiation, the term "simple" goiter included a large percentage of cases without toxic symptoms, and a small percentage with toxic symptoms (toxic non-exophthalmic, group 1). There is no doubt that the term "simple" goiter should be dropped, and the term "atoxic" substituted as covering the majority of the cases, while those cases which present any toxic symptoms should be described as "toxic non-exophthalmic."

The operative treatment for the uncomplicated non-toxic thyroid is approximately the same as that for the simpler types of exophthalmic goiter, section of the muscles not often being required, however. Operations on adenomas, colloid thyroids, or diffuse adenomatoses, as a rule, involve but slight risk to the life of the individual. Many patients who are so afflicted wish to be relieved of the deformity, tracheal pressure, hoarseness, or possibly of a severe neuralgia.

Intrathoracic goiters and deep substernal goiters are of serious import, and are found about once in 40 operations for simple goiter. Slight substernal projections are much more frequent. The diagnosis rests on—(1) Dull area on percussion; (2) the roentgenogram, and (3) evidence of substernal pressure. Probably one-sixth of the original gland-cells are competent to furnish all secretion necessary. It is best, therefore, to preserve this much of the gland until there is more evidence furnished that all of it can be removed with no ill effects, as is claimed by some surgeons in their treatment of exophthalmic goiter.

Malignant tumors of the thyroid are not numerous. Less than 1 per cent. of the cases operated on in our clinic show malignancy. Both cancer and sarcoma occur, the former with much more frequency. The diagnosis should, if possible, be made before the growth has penetrated the capsule and involved the neighboring structures, for example, the trachea and muscles. The only treatment which affords any hope of relief is free removal of the entire thyroid tissue. Unfortunately, early glandular and lung metastases are common. In most cases the growth has proceeded beyond

its capsule before the patient comes to the surgeon, and the ultimate results are not promising. When recurrence takes place, the process is more rapid than before operation.

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## THE PATHOLOGY OF THE THYROID IN EXOPHTHALMIC GOITER \*

LOUIS B. WILSON

The studies on which the present paper is based are a continuation of those first reported to the Association of American Physicians five years ago. At that time I gave a detailed analysis of the pathologic examination of 259 thyroids removed from patients listed as "exophthalmic goiter" in the Mayo Clinic from January 1, 1905, to May 10, 1908, and, in addition, a review of the pathologic reports on 35 cases similarly listed prior to January 1, 1905. While these cases were not all such as we would now diagnosticate exophthalmic goiter, they were all toxic, and probably contained as high a percentage of cases of true exophthalmic goiter as could have been found in any clinical list at that time.

The solution of problems of the pathology of the thyroid has long been rendered more difficult by indefinite clinical diagnoses and nomenclature, and this no doubt accounts for much of the disagreement between workers in different clinics. While non-toxic cases usually have been diagnosed clinically "simple goiter," and cases with marked symptoms have been diagnosed "exophthalmic goiter," yet many cases with mild symptoms have also been called "simple goiter," and many cases, though not true exophthalmic, yet markedly toxic, have been called by most clinicians "exophthalmic goiter."

Though a sharp distinction between the two clinical types of toxic cases—exophthalmic and non-exophthalmic—had not been

\* Presented before the Association of American Physicians, Washington, D. C. May 7, 1913. Reprinted from *Amer. Jour. Med. Sci.*, December, 1913, pp. 781-790. Copyright, 1913, by Lea and Febiger.

made in 1908, I was able to show that pathologically there were two distinct types of glands to be found among thyroids removed from toxic goiter cases. While purposely avoiding as much as possible previously used technical terms, I attempted to simplify our conception of the pathology by pointing out that the essential element in a large percentage of the cases was an increase in the amount of working tissue—parenchyma cells—within the previously formed acini, or, in other words, hypertrophies, hyperplasias, and regenerations, while in a smaller percentage of the cases there was an apparent increase in the amount of working tissue—parenchyma, due to an increase in the number of acini, or, in other words, adenomas, adenomatoses, etc. Class I, containing the hypertrophies, hyperplasias, and extreme regenerations, constituted 79 per cent. of the total number of specimens examined, while Class II, containing the fetal and colloid adenomas, the adenomatoses, and the so-called simple colloid thyroids, constituted 21 per cent. of the specimens examined.

In comparing my theoretic estimate of the stage and severity of the disease, as indicated by the above data, with the clinical facts as previously observed and noted by Plummer, it was shown that a direct relationship existed between the apparent functional activity of the gland and the stage and severity of the clinical symptoms. In reviewing the clinical data of his more recent cases, Plummer has found that practically all, if not all, the cases of clinically true exophthalmic goiter lie in the pathologic groups showing hypertrophy and hyperplasia, while the toxic non-exophthalmic cases are scattered among the other pathologic groups. We have, however, up to the present time, continued the ordinary method of listing clinically all severe toxic goiter cases closely resembling exophthalmic cases on the "exophthalmic goiter" list, while on the simple goiter list are placed those cases in which there are slight or no acute toxic symptoms. Our "exophthalmic goiter" list, therefore, contains those cases coming to our clinic which are ordinarily diagnosed exophthalmic goiter, but which Dr. Plummer divides clinically into two classes—exophthalmic toxic and severe non-exophthalmic (*i. e.*, non-hyperplastic) toxic.

I have recently reviewed all the gross and microscopic fixed tissue at hand from the cases reported in 1908, and, in addition, have studied grossly and microscopically in fixed tissues all the glands available which have been removed between May 10, 1908, the date of my previous report, and January 1, 1913, from all patients on our "exophthalmic goiter" list. This includes a total of 1208 thyroids from patients, all of whom had shown marked toxic symptoms, though not all of whom, in the light of our present clinical knowledge, would now be diagnosed true exophthalmic goiter. In addition to these 1208 glands from toxic cases, I have similarly studied the glands removed during the year 1912 from cases grouped clinically as "simple goiters"—585 in all. These latter 585 thyroids are from patients presenting very slight or no acute toxic symptoms. I have further studied the thyroids from a number of human embryos and from children, adolescents, and adults coming to autopsy without clinical history of thyroid derangement. My observations on the latter groups will be presented in later papers.

In order to maintain a standard of comparison in the analyses of these cases it has been found necessary to adopt numeric equivalents for amount, size, degree, etc., and the analytic data thus designated have been tabulated on forms parallel in size and arrangement of names with those used by Plummer for the tabulation of the clinical data. The headings of the tables are shown in Table I.

All pathologic observations have been made wholly independently of the clinical observations, and not compared with the latter until the entire series was completed.

While many thyroids may each present a great variety of histologic pictures, yet a careful examination of a large number of sections from blocks of fixed tissue from different areas, combined with the examination of the gross specimens, permits one to classify the glands with considerable definiteness. In grouping the specimens I have classified them with but slight change on the basis which I adopted in 1908 and elaborated last year. Thus groups A, B, C, and D represent Class I, namely, the parenchymatous hypertrophies and hyperplasias and extreme regenerations, while

or tissue

GENERAL CHARACTERISTICS					
Secondary capsule	Hemorrhage	Degeneration	Cyst Size of	Bloodvessels Size of Larger	
Thin	0.	H-Hyaline	0-None		
Medium	1.	Ct-Cartilage	1-Small	1.	
Dense	2.	Mx-Myxomatous	2-Medium	2.	
Thick	3.	Cl-Calcareous	3-Large	3.	
	4.		4-V. Large	4.	
		0, 1, 2, 3, 4			
					1
					2

		DIAGNOSIS OF CLINICAL CONDITION			PROGNOSIS	OFFICE No.	
IN	Index of Total Circulating Secretion	Stage of Toxic Symptoms	Severity of Toxic Symptoms	Severity of Second- ary Changes	RT-Relief of Toxic Symptoms 0, 1, 2, 3, 4		
		0, 1, 2, 3, 4	0, 1, 2, 3, 4	0, 1, 2, 3, 4	RS-Relief of Secondary Symptoms 0, 1, 2, 3, 4		
							1
							2





groups E, F, G, and H represent Class II, namely, the “adenomas,” “adenomatoses,” and “colloid goiters.”

Hypertrophy and hyperplasia are almost always intermingled, but it is possible to subdivide the hypertrophies and hyperplasias into three classes: Group A, early primary parenchymatous hypertrophy and hyperplasia (see Fig. 248); Group B, active advanced primary parenchymatous hypertrophy and hyperplasia (see Fig.

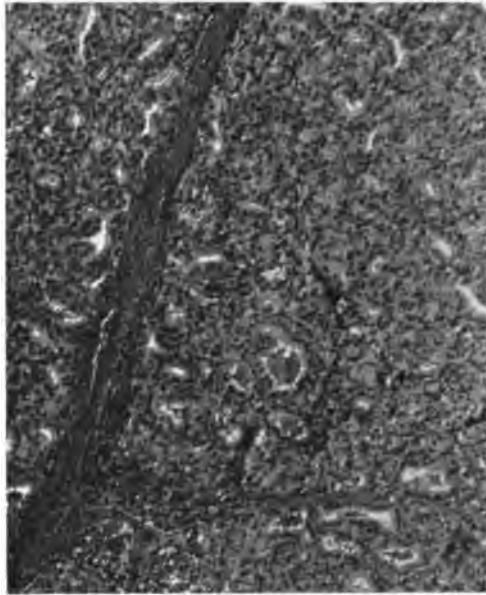


Fig. 248.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type A. Early primary parenchymatous hypertrophy and hyperplasia. From a case of clinically early true exophthalmic goiter.

249); Group C, regressing primary parenchymatous hypertrophy and hyperplasia. (See Fig. 250.) I have used the term “primary” in each of these classifications because I believe it represents a stage of hypertrophy and hyperplasia developing a parenchyma which previously has not been markedly atrophic. Group D contains those specimens in which a marked regeneration of parenchyma is found developing on apparently previously atrophic parenchyma lining the walls of previously distended, colloid filled

acini. (See Fig. 251.) This regeneration is marked by the presence of numerous minute acini lined with low spheric or cuboid epithelium, and filled quite early with densely staining colloid. Critically considered, the process is really a form of hyperplasia, and it is possible, indeed, for it to grade progressively over into primary hypertrophy and hyperplasia, but I have rigidly excluded from groups A, B, and C all glands which did not show marked

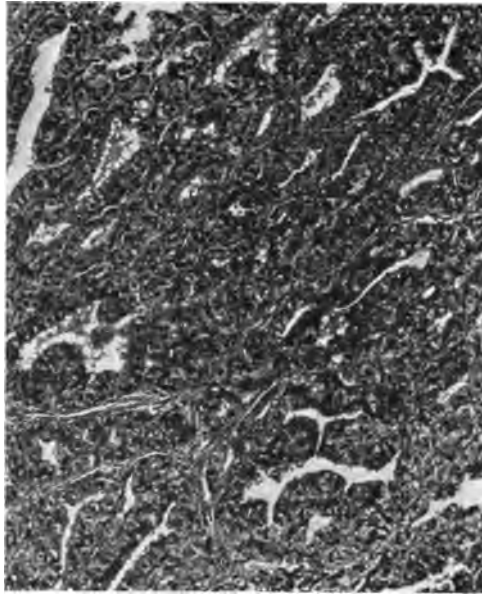


Fig. 249.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type B. Advanced primary parenchymatous hypertrophy and hyperplasia. From a case of clinically severe true exophthalmic goiter.

infolding of acinar walls lined with columnar epithelium. On the other hand, it is frequently impossible to draw the line between those degrees of regeneration in a colloid thyroid which might fairly be presumed to be the cause of toxic symptoms and those in which no effect can be noted. All that I have attempted here is to note in a study of the glands removed from known toxic cases the presence or absence of marked regeneration. While theoretically it would seem to be extremely confusing to differentiate

secondary regenerations from primary hypertrophies and hyperplasias, yet, as a matter of fact, when sections from material which has been properly fixed and stained are studied, the task is not a difficult one.

Of the groups in Class II, group E contains the actively growing, non-degenerating fetal adenomas (see Fig. 252); group F contains fetal adenomas, which show any of the several types of degeneration

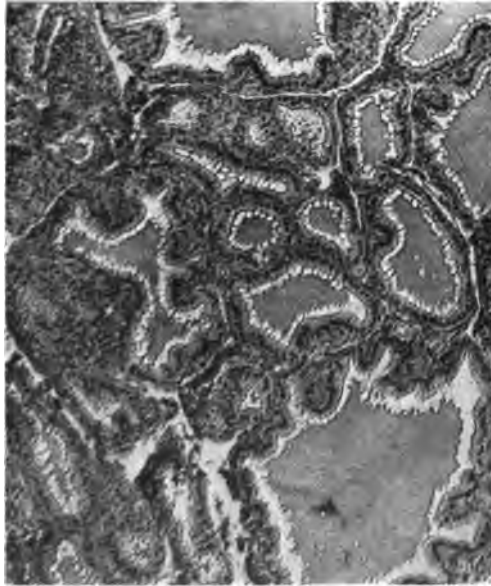


Fig. 250.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type C. Regressing primary parenchymatous hypertrophy and hyperplasia. From a case of clinically true exophthalmic goiter; late stage.

—myxomatous, hyaline, calcareous, etc. (see Fig. 253); group G contains those definitely encapsulated adenomas whose acini are too large to be classified as fetal and which may or may not be degenerated (see Fig. 254); and group H contains those thyroids not included in the previous classes, many of which, though not presenting definitely encapsulated tumors, yet are composed of more or less segregated groups of acini presenting a picture which,

following Adami's lead, I prefer to class as "adenomatoses." (See Fig. 255.)

The following table gives the classification of the thyroids studied according to the above grouping:

TABLE II.—PATHOLOGIC CLASSIFICATION OF THYROIDS FROM PATIENTS ON "EXOPHTHALMIC GOITER" LIST FROM JANUARY 1, 1905, TO DECEMBER 31, 1912, AND OF THYROIDS FROM PATIENTS ON "SIMPLE GOITER" LIST FOR 1912

"Exophthalmic Goiter" List.										"Simple Goiter" List.	
YEARS		1905	1906	1907	1908	1909	1910	1911	1912	Totals	1912
A	Early primary parenchymatous hypertrophy and hyperplasia.	..	1	4	2	1	3	15	6	32 3%	..
	Advanced primary parenchymatous hypertrophy and hyperplasia.	4	26	35	41	44	68	108	89	415 34%	1
C	Regressing primary parenchymatous hypertrophy and hyperplasia.	7	21	44	55	46	78	107	140	498 41%	3
Total hypertrophy and hyperplasia (A + B + C).		11 69%	48 83%	83 68%	98 69%	91 71%	149 77%	230 81%	235 89%	945 79%	4 4
D	Secondary regeneration of atrophic parenchyma of "colloid" goiter.	1 6%	3 5%	24 20%	24 17%	17 13%	30 15%	20 7%	14 5%	133 11%	50 9%
E	Fetal adenomas.	1	3	7	17	8	2	12	2	52 4%	35
F	Degenerating fetal adenomas.	3	3	5	3	5	12	21	10	62 5%	101
G	Adult ("colloid") adenomas.	..	1	1	..	6	1	..	3	12 1%	128
Total adenomas (E + F + G).		4 25%	7 15%	13 11%	20 14%	19 13%	15 7%	33 12%	15 6%	126 10%	264 44%
H	Atrophic parenchyma ("colloid") thyroids "adenomatoses," etc.	..	..	1	..	1	2	..	..	4	259 44%
	Malignant tumors.	..	..	..	..	..	..	..	..	8 14%	..
Total number of thyroids.		16	58	121	142	128	196	283	264	1208	585

A study of the table reveals the following interesting points:

1. Approximately four-fifths, 79 per cent., of all thyroids from patients who had exhibited sufficiently severe acute toxic symptoms to warrant the clinician in placing them on the "exophthalmic goiter" list, showed marked hypertrophy or hyperplasia, or, more usually, both.

2. During the year 1912 this percentage rose to 89. At the same time, a parallel examination by the same observer of 585 thyroids from patients on the "simple goiter" list for 1912 showed but four cases—less than 1 per cent.—with hypertrophy and hyperplasia. Of these four cases, three were children and one was a young adult female whose lack of toxic symptoms can be accounted for only on the hypothesis that she was highly resistant and had not yet had time to be affected.

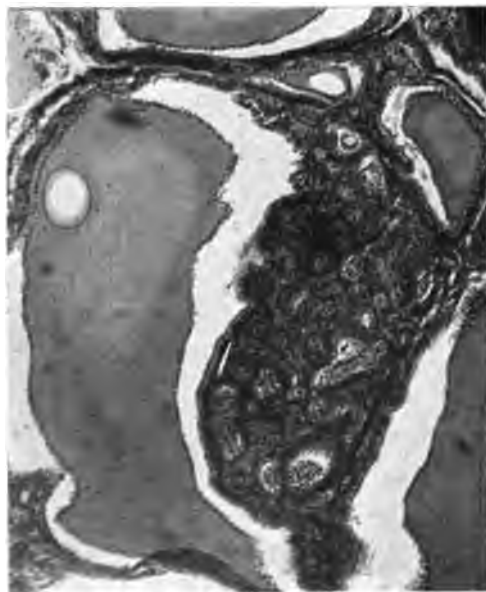


Fig. 251.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type D. Secondary regeneration of atrophic parenchyma. From a case of clinically toxic non-exophthalmic goiter.

3. During the years 1911 and 1912 every patient diagnosed clinically as true exophthalmic goiter and on whom thyroidectomy was done, furnished thyroid tissue which pathologically was placed in the groups marked A, B, or C, that is, showing primary parenchymatous hypertrophy and hyperplasia.

4. So far as can be determined none of the 133 patients—11 per cent.—whose thyroids showed only secondary regeneration of

atrophic parenchyma would now be classified clinically, according to Plummer, as true exophthalmic goiter. This distinction is clinically sharp and positive for the years 1910, 1911, and 1912, and not yet critically reviewed from the clinical standpoint for the preceding years.

5. The statement in paragraph 4 is equally true for the 130 cases—10 per cent.—whose thyroids are grouped as E, F, G, or H (adenomas, etc.).

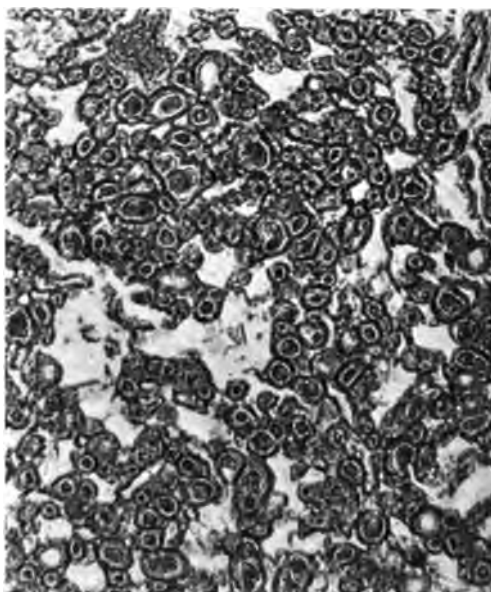


Fig. 252.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type E. Fetal adenoma. From a case of clinically toxic non-exophthalmic goiter.

6. At the same time these groups D, E, F, G, and H—regenerations, adenomas, colloids, etc.—contain 97 per cent. of all thyroids removed from patients on the “simple goiter” list for 1912.

In attempting to estimate from the pathologic data alone the stage of the toxic clinical symptoms, the following factors have been taken into account: (1) Age of the patient, (2) weight of the portion of gland removed; (3) character of the blood-vessels; (4) amount

of stroma; (5) size and shape of the acini; (6) amount of hypertrophy and hyperplasia of the parenchyma cells; and (7) amount and density of the secretion contained within the acini. These factors must all be considered in estimating the product and output of the gland so far as may be made from a pathologic examination of the tissues. A careful consideration of all these factors has been made in each case examined, and a tentative estimate given of the stage and severity of the disease at the time the patient was oper-

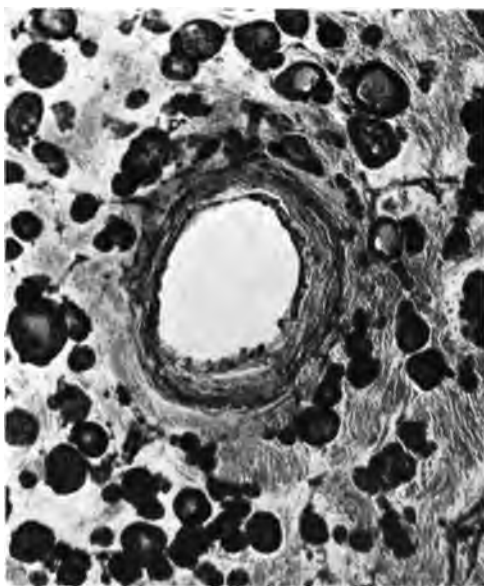


Fig. 253.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type F. Degenerating fetal adenoma. From a case of clinically toxic non-exophthalmic goiter.

ated on. These estimates have been compared in parallel columns with the clinical estimates made by the examining physician for all cases operated on during 1910, 1911, and 1912 (the only years for which the full clinical data, except of those given in my paper of 1908, have as yet been critically reviewed). The results may be briefly summarized as follows:

1. Of the 24 cases diagnosed pathologically as Group A (early

primary parenchymatous hypertrophy and hyperplasia), 21 (87.5 per cent.) had exhibited symptoms for but three months or less.

2. Of the 265 cases placed pathologically in Group B (advanced primary parenchymatous hypertrophy and hyperplasia), 11 (4 per cent.) gave a history of toxic symptoms for but three months, 155 (58 per cent.) from three months to one year, 34 (13 per cent.) (almost all young individuals) slightly over a year, but with a

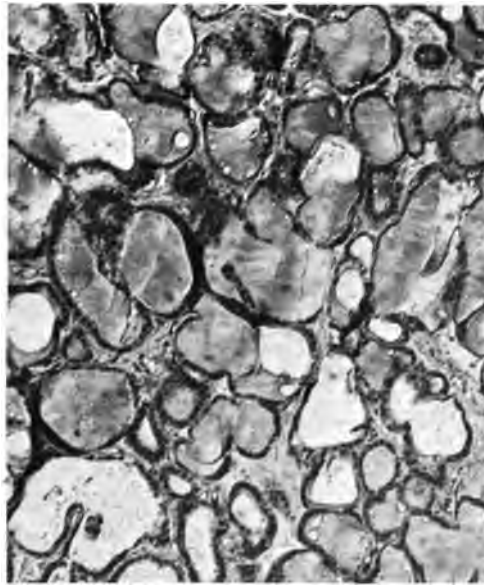


Fig. 254.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type G. Adult, "colloid" adenoma. From a case of clinically toxic non-exophthalmic goiter.

ligation shortly preceding thyroidectomy, while 65 (24.5 per cent.), these again almost all young individuals, had exhibited symptoms for over a year and had had no ligation previous to thyroidectomy.

3. Of the 325 cases diagnosed pathologically as group C (regressing primary parenchymatous hypertrophy and hyperplasia), 8 (2 per cent.) gave a history of but three months' duration of symptoms (and without ligation prior to thyroidectomy), 25 (8 per cent.) gave a history of one year or less duration of symptoms



(and without ligation prior to thyroidectomy), while the remainder, 292 (90 per cent.), gave clinical histories of more than one year's duration or had had a ligation some weeks before the performance of thyroidectomy.

Thus it will be seen that notwithstanding the inaccuracies of patients' statements as to the duration of symptoms, notwithstanding the confusing factor of a ligation previous to thyroid-

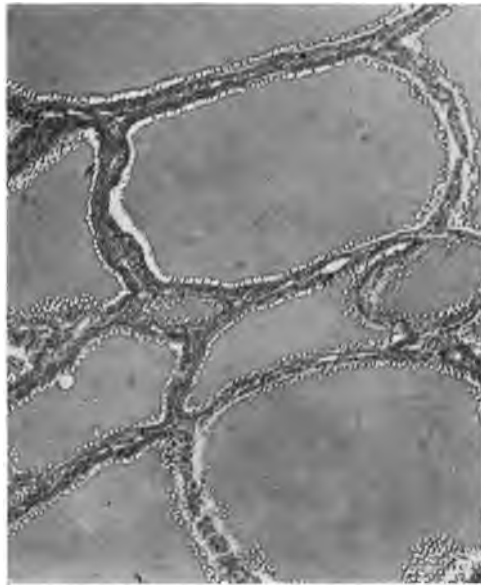


Fig. 255.—Photomicrograph of a section of thyroid ( $\times 120$ ). Type H. "Colloid thyroid." From a case of clinically non-toxic goiter.

ectomy, and notwithstanding the difficulties of correctly estimating the total function from an anatomic study of but a portion of a gland, the fact remains that the stage of true exophthalmic goiter can be estimated with considerable accuracy from the pathologic data alone in about 80 per cent. of all cases examined.

In attempting to estimate the severity of the toxic symptoms in the cases with true exophthalmic goiter, all of which had shown pathologically some stage of hypertrophy and hyperplasia in the

thyroid (Groups A, B, or C), the same factors were taken into consideration as those entering into the estimate of the stage of the disease. A careful consideration of these data resulted in the classification of the cases for 1910, 1911, and 1912 into the four grades of severity: (1) Very mild; (2) moderate; (3) severe; (4) very severe. On only 542 cases out of the 614 was it possible to make a definite comparison of the estimated severity from the pathologic standpoint with the severity as noted by the clinician just prior to thyroidectomy.

Out of these 542 cases, 29 were estimated pathologically as "1," or of "mild" severity. Twenty-two out of the 29 had been previously similarly grouped by the clinician, or, in other words, the pathologic estimate agreed with the clinical findings in 76 per cent. of the cases in this group.

Of the 306 cases estimated pathologically as "2," or of "moderate" severity, 235 were similarly placed by the clinician, an agreement of 77 per cent. in this group.

Of the 166 cases estimated as of severity "3," that is, "severe," 117 were similarly grouped by the clinician, an agreement of 70 per cent.

Of the 41 cases estimated pathologically as severity "4," that is, "very severe," 33 have been similarly grouped by the clinician, an agreement of 80 per cent.

Thus of the 542 cases on which the degree of severity was estimated from the examination of pathologic specimens, such estimate agreed with the clinical estimate in 407 cases, or a total pathologic accuracy of 75 per cent.

#### CONCLUSIONS

1. A detailed pathologic study of fixed-tissue preparations from 1208 thyroids, removed from patients whose condition would ordinarily have been diagnosed exophthalmic goiter, showed that 79 per cent. of the thyroids contained large areas of marked primary hypertrophy and hyperplasia. A parallel clinical study has shown that for a period of three years all cases with true ex-

ophthalmic goiter, and from whom gland tissue was removed, fall into this list.

2. In the above series of 1208 so-called "exophthalmic goiters" plus 585 so-called "simple goiters," or a total of 1793 thyroids, but 4 instances of marked primary hypertrophy and hyperplasia of the parenchyma have been noted in cases which did not show clinical symptoms of true exophthalmic goiter. Three of these four patients were children.

3. Twenty-one per cent. of the 1208 glands were either regenerations or adenomas. Clinically, while all of these were markedly toxic, all were chronic and none of them would now be grouped clinically as true exophthalmic goiter.

4. By assuming that the symptoms of true exophthalmic goiter are the results of an excretion from the thyroid, and by attempting to determine the amount of such excretion from the pathologic data, one is able to estimate in a large series of cases the clinical stage of the disease with about 80 per cent. of accuracy and the clinical severity of the disease with about 75 per cent. of accuracy.

5. It would therefore appear that the relationship of primary hypertrophy and hyperplasia of the parenchyma of the thyroid to true exophthalmic goiter is as direct and as constant as is primary inflammation of the kidney to the symptom of true Bright's disease. Any considerable finding to the contrary I believe to indicate either inaccurate or incomplete observations on the part of the pathologist or clinician, or both.

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## NOTES ON THE PATHOLOGY OF SIMPLE AND EXOPHTHALMIC GOITER \*

LOUIS B. WILSON

I have recently reviewed the pathology of the thyroid glands removed from 1208 patients in the Mayo Clinic presenting symptoms which would ordinarily be diagnosed as exophthalmic goiter, and, for purposes of control, 585 thyroids removed during 1912 from patients whose condition would ordinarily be diagnosed as simple goiter. Some of the conclusions of more general interest to the clinical diagnostician and surgeon have been presented elsewhere. I wish to present here, however, certain data of interest more directly to the pathologist.

Much of the trouble in interpreting the pathology of the thyroid gland has come from the associated difficulty of the clinician in definitely grouping the clinical symptoms. Recently, however, Plummer has sharply differentiated the toxic symptoms of goiter into two clinical groups: First, toxic exophthalmic, and, second, toxic non-exophthalmic. Plummer points out that, aside from, sooner or later, exhibiting the symptom of exophthalmos, the cases of the first group are acute, and, in many respects, resemble the symptoms of acute alcoholism, while those of the second group are chronic and, in many respects, parallel the train of symptoms associated with arteriosclerosis from chronic alcoholism. In this latter group are many cases so mildly or so aberrantly toxic that clinicians in the past have frequently listed them as simple goiters. Plummer suggests that this latter term should be aban-

\* Read by title before the American Association of Pathologists and Bacteriologists, Washington, D. C., May 7, 1913. Reprinted from the Medical Record, August 30, 1913, pp. 373-378.

done by the clinician and in its place should be substituted the term non-toxic.

*Technic.*—While, by the study of freshly removed thyroids grossly it is possible to determine the general contour of the gland, the presence or absence of encapsulated adenomas, the relative amount of gross degenerations and the consistence of the fresh colloid, and while it is also possible to differentiate marked primary

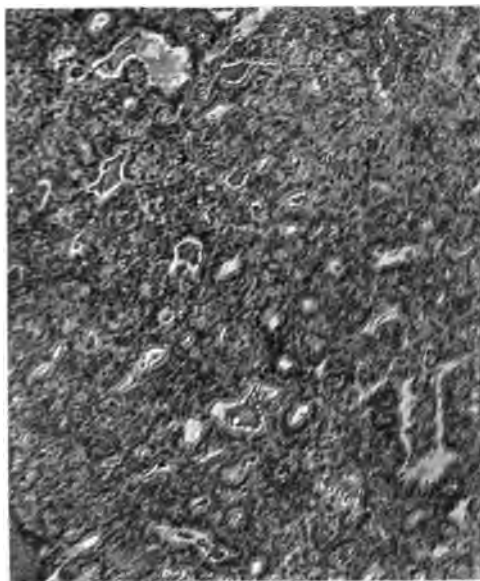


Fig. 256.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type A. Early primary parenchymatous hypertrophy and hyperplasia. From case of clinical early exophthalmic goiter.

hyperplasias, adenomas, etc., in properly stained frozen sections of perfectly fresh tissues, yet any careful estimate of the amount of hypertrophy, hyperplasia, atrophy or regeneration of the parenchymal cells, of the size of the acini, of the amount of the contained colloid and its density as indicated by its staining reaction, as well as the variation in most of the finer details of the cells themselves, must all come from the study of good sections of fixed tissues. Zenker's fluid, 10 per cent. formalin, and Bensley's

chromosmic mixture are the best and most convenient fixatives for routine work.

While there is some shrinkage of the less dense colloid in even the most carefully prepared paraffin sections, yet this is less confusing than the error due to the use of celloidin as an embedding medium, since the stainability and refractive index of the latter are frequently so near that of the colloid that the two are indistinguishable.

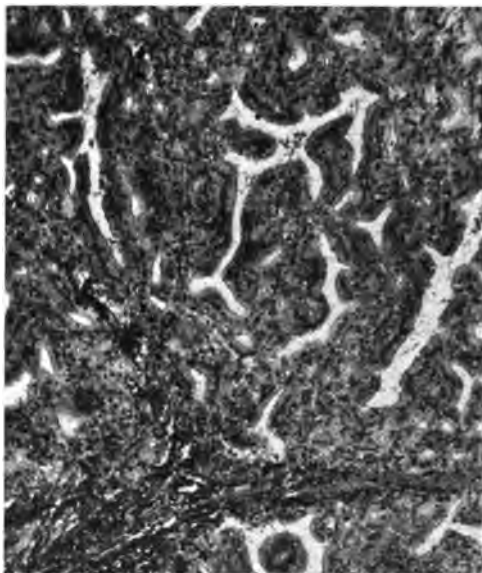


Fig. 257.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type B. Advanced primary parenchymatous hypertrophy and hyperplasia. From case of clinical severe exophthalmic goiter.

The most desirable stain we have tried for routine examinations is Weigert's hematoxylin, followed by Van Gieson's picric acid and acid fuchsin.

Since each thyroid gland consists of an enormous number of acini, each of which is capable of taking on changes quite distinct from those found within the acini adjoining it, it is only by the selection of representative blocks from a large number of areas, by the study of a number of sections from each block, by the

tabulation of the detailed results of such study, and, finally, by the summary of this tabulation that one may hope to arrive at any fairly accurate estimate of the total hyper- or hypo-function of the gland which will enable him to state the clinical condition of the patient from whom the gland was removed. In my studies I have used a scheme of tabulation indicated by the column headings in Table I (opposite page 514).

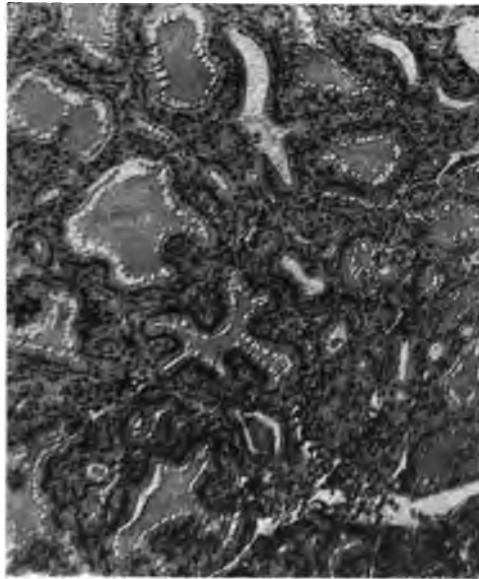


Fig. 258.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type C. Regressing primary parenchymatous hypertrophy and hyperplasia. From case of clinical exophthalmic goiter, late stage.

The character of the data and the method of recording are here indicated and need no further discussion. On the tabulation sheets the patients have been arranged in the same order as that maintained on the sheets on which were tabulated the clinical data concerning the same patients. This has made it a relatively simple matter finally to coördinate the clinical and pathologic data, a process which, with any large number of patients, becomes almost impossible without some prearranged plan.

In the interpretation of the pathologic data I have followed the hypothesis that the symptoms of true exophthalmic goiter, if not due to, are at least constantly associated with, an overproduction of an absorbable secretion within the thyroid gland. The presence of such a hypothetic secretion within the blood of the patient suffering from symptoms of exophthalmic goiter has not yet been positively proved, though the work of Blackford and Sanford on the depressor action of extracts of fresh thyroid and

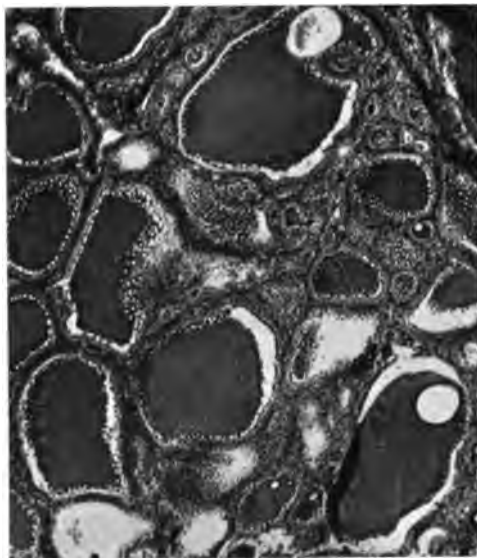


Fig. 259.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type D. Secondary regeneration of atrophic parenchyma. From case of clinical toxic non-exophthalmic goiter.

of the serum from exophthalmic goiter patients goes far to establish the hypothesis of the existence of such a substance within the blood of toxic exophthalmic goiter cases.

*Classification of Histologic Conditions of the Thyroid.*—The following classification of the histologic conditions met with in the thyroid has been followed in these studies:

- I. Embryonic (undeveloped) thyroid.
- II. Normal (resting) thyroid.



### III. Vascular changes.

1. Hyperemia.
2. Hemorrhage (including resulting cyst formation).

### IV. Inflammations.

#### V. Progressive changes.

1. Hypertrophy (functional, with hyperemia).
2. Hyperplasia ("exophthalmic" goiter).
3. Adenomatosis (multiplication of acini without encapsulation).
4. Regeneration of previously atrophic parenchyma).

#### VI. Retrogressive changes.

1. Retention of secretion (colloid goiter).
2. Atrophy of parenchyma).
3. Degenerations.
  - (a) Colloid (of parenchyma and stroma).
  - (b) Hyaline.
  - (c) Amyloid.
  - (d) Calcareous.
  - (e) Cystic.

### VII. Tumors.

1. Benign.
  - (a) Fetal adenomas (encapsulated).
  - (b) Adult adenomas (encapsulated).
2. Malignant.
  - (a) Mesotheliomas.
  - (b) Carcinomas.
  - (c) Sarcomas.

So far as the pathology of the two toxic types of goiter and the non-toxic is concerned, the chief lesions of the thyroid to which attention must be given are hypertrophy, hyperplasia, regeneration and atrophy of the parenchyma, retention of secretion, and the formation of adenomas.

*Hypertrophy and Hyperplasia* (See Figs. 256, 257, and 258).--Hypertrophy of the parenchyma, as indicated by the presence of large-cell columnar epithelium, with nuclei approaching the free extremities of the cells, was present in the parenchyma of the

glands from all the 945 cases of true exophthalmic goiter examined. On the other hand, it was found in the glands from but 4 of the 485 cases of so-called "simple goiter" operated on during the year 1912. Similarly, hyperplasia was found in the glands from every one of the 945 cases of true exophthalmic goiter, being present in 926 cases—98 per cent. On the other hand, it was present in less than 1 per cent. of the specimens examined from the 585 cases of so-called "simple goiter" operated on during 1912.

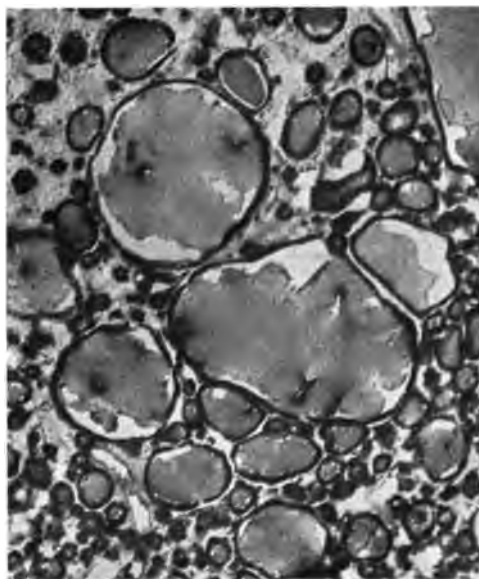


Fig. 260.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type E. Fetal adenoma with some acini distended with colloid. From case of clinical toxic non-exophthalmic goiter.

Hypertrophy and hyperplasia are marked by a progressive increase in the size of the acini. Thus, of the 32 glands which are marked as A (early parenchymatous hypertrophy and hyperplasia), the average size of the acini is indicated as 2 (medium), of the 412 glands grouped as B (active advanced primary parenchymatous hypertrophy and hyperplasia) the average size of the acini is  $2\frac{1}{2}$  (medium to large), while in the 499 thyroids grouped as C (re-

gressing primary parenchymatous hypertrophy and hyperplasia), the average size of the acini is 3 (large).

The shape of the acini also varies directly as to the amount of hypertrophy and hyperplasia. Thus, of the 945 cases examined, the irregularity is noted as 2 (moderate), or greater, in 933 cases (99 per cent.), while projection of papillæ within the acini is noted as 2 (moderate), or greater, in 852 cases (90 per cent.).

In hypertrophic thyroids the cytoplasm becomes more granular as the cells become more columnar. A careful study of this characteristic of the cells was made of the specimens obtained during 1911 and 1912 from exophthalmic goiter cases. Of the 363 glands studied, 291 (90 per cent.) showed very marked granularity of the cytoplasm.

The nucleus is nearly always swollen in the columnar epithelium. Thus, of the 364 cases studied consecutively with this point in view during 1911 and 1912, 361 (99 per cent.) showed that wherever the epithelium approached the columnar type, the nuclei were perceptibly swollen. The staining reaction of the nucleus is almost invariably intensified in hyperplastic parenchymal cells.

The amount of the secretion within the acini varies with the stage of the disease in true exophthalmic goiter. Thus 75 per cent. of the cases of group A (early primary parenchymatous hypertrophy and hyperplasia) are marked 0, 1, or 2 (absent, small, or moderate), 96 per cent. of the cases marked B (advanced active parenchymatous hypertrophy and hyperplasia) have the amount of secretion indicated as 1, 2, or 3 (small, moderate, or large), while 95 per cent. of the cases marked C (regressing parenchymatous hypertrophy and hyperplasia) have the amount of secretion within the acini indicated as 2, 3, or 4, that is, as moderate, large, or very large.

Similarly, the density of the secretion varies with the stage of the disease. Thus, of the cases of group A (early parenchymatous hypertrophy and hyperplasia), 75 per cent. gave a staining reaction of the secretion in fixed tissue which is indicated as 0, 1, 2 (absent, slight, or moderate), while of the specimens in group B (advanced parenchymatous hypertrophy and hyperplasia) 98 per cent. are

similarly marked, but of the cases in group C (regressing parenchymatous hypertrophy and hyperplasia), 75 per cent. are marked as 2, 3, or 4 (moderate, marked, or very marked) degrees of density.

The hypertrophy of the parenchymal cells is indicated grossly in the gland by a total increase of tissue from two to ten times the normal weight. The average weight of the portion of thyroid removed from our cases of group A (early primary parenchymatous hypertrophy and hyperplasia) was 38 grams, the average weight

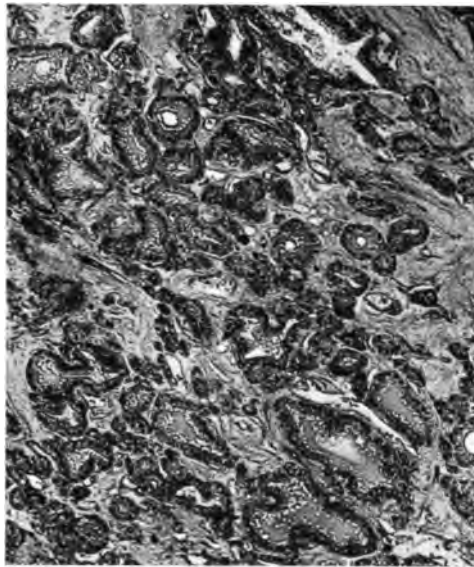


Fig. 261.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type F. Degenerating fetal adenoma. From case of clinical toxic non-exophthalmic goiter.

of the portion of gland removed from the cases of group B (active advanced parenchymatous hypertrophy and hyperplasia) was 61 grams, and the average weight of the portion of glands removed of group C (regressing primary parenchymatous hypertrophy and hyperplasia) was 51 grams, while the average for the entire series of glands of the three types (groups A, B, and C) of primary parenchymatous hypertrophy and hyperplasia was 55 grams.

While the increase in size of the gland in all cases operated on

of primary parenchymatous hypertrophy and hyperplasia is marked, the total weight of the gland is not as great as of those removed from cases of non-toxic or toxic non-exophthalmic goiters. For example, the average weight of the portion of gland removed from the patients with severe toxic non-exophthalmic goiter (but on "exophthalmic goiter" list) was 77 grams, while the average weight of the portion of gland removed from the non-toxic and aberrantly toxic cases ("simple goiter" list) of 1912 was 159 grams.

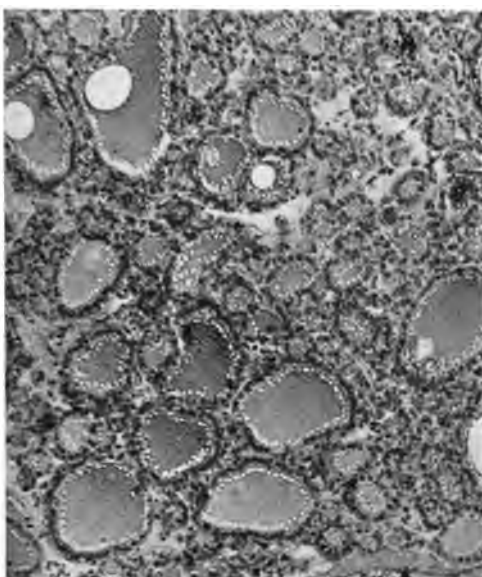


Fig. 262.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type G. Adult "colloid" adenoma. Note dense colloid in small acini. From case of clinical toxic non-exophthalmic goiter.

*Regeneration of Parenchyma* (See Fig. 259).—There is abundant evidence to show that thyroid parenchyma which has been atrophic may later regenerate. When such a regeneration occurs in previously markedly atrophic epithelium, it is usually only along one side of an acinus. In this situation there is a marked increase in the number of cells, which, however, as a rule, do not show any considerable increase in size (hypertrophy), but tend to remain embryonic or cuboid in shape. There is also a much greater ten-

dency to form small embryonic acini than exists in the primary hyperplasia which has occurred on normal epithelium. These acini, while still small, are filled with colloid secretion, usually quite dense in character. It is probable that a reduced vascularity of the acinar walls is responsible not only for the relatively small size of the parenchymal cells, but also for the failure of absorption of the secretion and its consequent retention within the acini. It is sometimes, though not frequently, impossible to distinguish advanced regeneration from advanced regression in a primary parenchymatous hypertrophy and hyperplasia. As a rule, however, the general condition of the gland and the absence of columnar cells and of remains of papillæ will serve to differentiate the two.

Regenerations are characteristic of clinical cases presenting a history of long-standing enlargement of the thyroid with subsequent slowly developing toxic symptoms. Eleven per cent. of our cases which were sufficiently toxic to warrant placing them on the "exophthalmic goiter" list, as previously explained, were pathologically of this type.

*Adenomas and Adenomatoses* (See Figs. 260, 261, and 262).—Definitely encapsulated tumors within the body of the thyroid are frequently met with. They occurred in 10 per cent. of the thyroids from our cases on the "exophthalmic goiter" list and in 44 per cent. of our cases on the "simple goiter" list. While the significance of these tumors is still undetermined, for the present we should sharply differentiate them pathologically from the so-called adenomatoses. The connective tissue of the thyroid is not evenly distributed normally. Any local increase of the stroma tends to segregate groups of acini, and these may at the same time multiply. But I believe, however, we should not apply the term adenoma to these conditions unless there is a distinct encapsulation of the mass.

*Colloid Thyroid* (See Fig. 263).—The thyroid gland, in which the parenchyma consists of atrophic epithelium and in whose acini there is a large amount of thick colloid secretion, is ordinarily spoken of as a "colloid thyroid," providing it does not present the appearance of an encapsulated tumor. Less than 1 per cent. of our cases on the "exophthalmic goiter" list were of this type,

while 44 per cent. of our cases on the "simple goiter" list are so classified pathologically.

The table on p. 540 gives the grouping of the cases studied for purposes of this report.

*Estimation of the Stage and Severity of Toxic Clinical Symptoms.*—In estimating from the pathologic data alone the stage of the toxic clinical symptoms, the age of the patient, weight of the

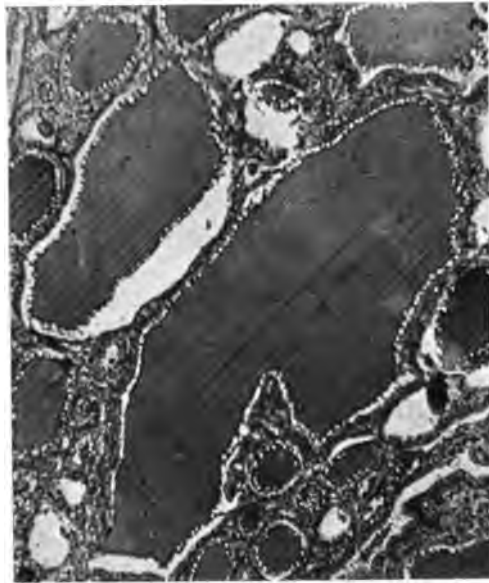


Fig. 263.—Photomicrograph of section of thyroid ( $\times 120$  diam.). Type H. "Colloid thyroid." From case of clinical non-toxic goiter.

portion of gland removed, character of the blood-vessels, amount of stroma, size and shape of the acini, amount of hypertrophy and hyperplasia of the parenchyma cells, and the amount and density of the secretion contained within the acini were all considered. Estimates made from the above data have in our series agreed with the clinical description of the stage of the disease in about 80 per cent. of all the cases examined. The same data were also considered in estimating the severity of the toxic symptoms in the cases

of true exophthalmic goiter. Such an estimate, made on 542 of the cases in our series, agreed with the clinical diagnosis in 75 per cent. of the cases.

#### SUMMARY

1. A detailed pathologic study of fixed-tissue preparations of the thyroids removed from adults and the finding thereby of marked primary parenchymatous hypertrophy and hyperplasia permits the pathologist to diagnose exophthalmic goiter with above 95 per cent. of accuracy. At the same time, a consideration of the data above mentioned will permit him to estimate the stage of the disease in about 80 per cent. of the cases and the severity of the disease in about 75 per cent. of the cases.

2. A similar study of thyroids from adult patients and the finding thereby of no marked hypertrophy, hyperplasia, or regeneration of parenchyma will permit the pathologist to diagnose non-toxic goiter with about 75 per cent. of accuracy.

3. The most difficult cases to diagnose pathologically are those of the clinical toxic non-exophthalmic type. While these are not hyperplastic, they may fall into any of the other above-mentioned groups. Our knowledge of these cases is still too incomplete to permit us to draw conclusions concerning the details of their pathology.

4. On the whole, it would appear that the pathologist has quite as much data for the estimation of the clinical symptoms of exophthalmic goiter from the pathologic data to be obtained from a study of the thyroid as he has to estimate the clinical symptoms of Bright's disease from the pathologic data to be obtained from the study of the kidney.

#### REFERENCES

- Blackford and Sanford: *Trans. Assoc. Amer. Phys.*, 1913; also *Amer. Jour. Med. Sci.*, vol. cxlvi.  
Plummer: *Trans. Assoc. Amer. Phys.*, 1913; also *Amer. Jour. Med. Sci.*, 1913.  
Wilson: *Trans. Assoc. Amer. Phys.*, 1913; also *Amer. Jour. Med. Sci.*, 1913.



## THE RELATION OF THE PATHOLOGY AND THE CLINICAL SYMPTOMS OF SIMPLE AND EXOPHTHALMIC GOITER \*

LOUIS B. WILSON

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I have recently reviewed in fixed tissues the pathology, both gross and microscopic, of all the thyroid glands now in the laboratories of the Mayo Clinic which have been removed from patients on the "exophthalmic goiter" list from January 1, 1905, to January 1, 1912, a total of 1208 exophthalmic thyroids. My report on these specimens has been published elsewhere.† I have also examined, in the same manner, all the thyroids now in the laboratory removed from patients on the clinical "simple goiter" list from January 1, 1905, to June 1, 1913, a total of 2356 simple goiters.

The clinical grouping of these cases is not so simple as would be indicated by the two lists, "exophthalmic" and "simple." While the lists express their clinical grouping as the cases would ordinarily be arranged in most clinics, Plummer‡ has recently differentiated the goiters into three clinical groups—A, true exophthalmics, distinguished by relatively rapid development, exophthalmos, etc.; B, toxic non-exophthalmics, distinguished from the preceding by slow development, absence of exophthalmos, etc.; and C, non-toxic goiters, distinguished from both of the preceding by entire absence of toxic symptoms. It is, therefore, necessary to remember that in our "exophthalmic goiter" list 79 per cent. are true exophthalmics, 21 per cent. are toxic non-

\* Read before the section on Pathology and Physiology, American Medical Association, Minneapolis, Minn., June 19, 1913. Reprinted from Jour. Amer. Med. Assoc., January 10, 1914, pp. 111, 112.

† Amer. Jour. Med. Sci., December, 1913, pp. 781-790.

‡ Plummer: Amer. Jour. Med. Sci., December, 1913, pp. 790-796.

exophthalmics, and in the "simple goiter" list 17 per cent. are toxic non-exophthalmics and 83 per cent. are non-toxic.

Each acinus of the thyroid gland can take on changes unlike those found within those adjoining it. It is hence necessary, in attempting to determine the dominant pathologic condition of the gland for purposes of classification, to make a detailed analysis from the study of sections from many areas, and finally to summarize the tabulated record of the observations. Such a summary can best be made from a tabulation in which numeric equivalents are used wherever possible to indicate degrees, amount, etc. Without going into the minutia of the specimens which I have examined, I wish to present herewith a broad summary of the results:

CLASSIFICATION (IN PERCENTAGES) OF THE PRINCIPAL PATHOLOGIC CHANGES IN 3564 THYROIDS REMOVED AT OPERATION FOR GOITER

1208 THYROIDS FROM PATIENTS ON "EXOPTHALMIC GOITER" LIST	PRINCIPAL PATHOLOGIC CHANGES	2356 THYROIDS FROM PATIENTS ON "SIMPLE GOITER" LIST
Clinically true exophthalmic goiter. { 79% (3%) (34%) (41%)	Primary hypertrophy and hyperplasia of parenchyma. A. Early. B. Advanced. C. Regressing.	0.6% {
Clinically toxic non-exophthalmic goiter. { 11% 10% (4%) (5%) (1%)	Secondary regeneration of atrophic parenchyma. D. Adenomas. E. Fetal. F. Degenerating fetal. G. Adult.	9% {
	Primary atrophy of parenchyma. H. Adenomatoses, Diffuse Colloids, etc. Malignant tumors.	45% { (6%) (17%) (22%) 44% 1.5%
		Clinically 17 per cent. toxic-non-exophthalmic goiter and 83 per cent. non-toxic goiter

An examination of the preceding table will reveal the following salient points:

1. Practically all cases of clinically true exophthalmic goiter show marked primary hypertrophy and hyperplasia of the parenchyma of the thyroid gland. Furthermore, as I have shown else-

where,\* the clinical stage of development of the disease is paralleled by the stage of development of the pathologic condition in sufficiently marked degree that one may estimate the clinical condition from the pathologic examination with about 80 per cent. of accuracy. The degree of severity of the clinical condition is similarly paralleled by the pathologic condition of the gland. The relationship between hypertrophy and hyperplasia of the thyroid gland and the clinical symptoms of true exophthalmic goiter is remarkably constant.

2. While mild degrees of hypertrophy and hyperplasia within physiologic limits may be present in the thyroid gland, particularly in the young and during pregnancy, yet the absence of this condition in the thyroids of adults coming to operation for toxic non-exophthalmic and non-toxic goiters is most striking. Without making any allowance for either clinical or pathologic errors of diagnosis, less than 1 per cent. of all cases coming to operation for goiter show any considerable primary hypertrophy and hyperplasia of the parenchyma of the thyroid, except as associated with clinical symptoms of true exophthalmic goiter.

3. Eleven per cent. of all the thyroids on the "simple goiter" list showed as their principal pathologic change a secondary regeneration of atrophic parenchyma. This secondary regeneration of atrophic parenchyma is marked by the development, usually on one side of an acinus, of multiple, small, new acini composed of embryonic or cuboid epithelium surrounding a minute cavity in which is found a very small amount of usually quite densely staining colloid. This newly developed tissue may extend out into the acinus in an irregular mass which can usually be readily distinguished from the papillæ of a primary hypertrophy by the small size of its cells as compared with the very large columnar cells which mark the latter.

These secondary regenerations are almost invariably recent enlargements of old "colloid goiters" whose primary atrophy must have occurred years before.

\* Amer. Jour. Med. Sci., December, 1913, and New York Medical Record, August 30, 1913.

4. Besides the 11 per cent. of glands of this type noted on the "exophthalmic goiter" list, 9 per cent. of the glands on the "simple goiter" list were of the same type. All the thyroids from patients on the "exophthalmic goiter" list which showed secondary regeneration were from patients whose clinical symptoms were marked toxic non-exophthalmic. Similarly, about half of the thyroids on the "simple goiter" list showing secondary regeneration were from patients who clinically gave symptoms of toxic non-exophthalmic goiter. Thus, in all, above 75 per cent. of the thyroids showing secondary regeneration of atrophic parenchyma were associated clinically with symptoms of chronic toxic non-exophthalmic goiter. It would appear from this that the pathologist is safe in saying that a colloid goiter which presents a large amount of regeneration is from a patient presenting chronic toxic non-exophthalmic symptoms. It must be remembered, however, that in a large number of the glands the process is too indefinite to permit the pathologist correctly to estimate the clinical condition of the patient.

5. Ten per cent. of the thyroids from patients on the "exophthalmic goiter" list were composed principally of encapsulated adenomas. All these were from patients with clinically toxic non-exophthalmic goiter.

6. Forty-five per cent. of the thyroids from patients on the "simple goiter" list were composed principally of encapsulated adenomas. More than half of these are distinctly of the so-called fetal adenoma type; that is, they consist of acini made up of small cuboid or embryonic epithelium in spheroid or columnar groups without lumina. The term fetal adenoma is somewhat misleading, since the thyroid in late fetal life is made up almost entirely of acini with definite lumina.

The smaller portion of the adenomas contains so many acini with lumina that one is not warranted in classifying them at all as fetal, and I have consequently grouped them as adult adenomas.

7. Less than half of 1 per cent. of the thyroids from patients on the "exophthalmic goiter" list, but more than 44 per cent. of the thyroids from patients on the "simple goiter" list, consist

principally of groups of dilated acini filled with thick, densely staining colloid material and lined with atrophic parenchyma. While many of these show varying amounts of stroma, more or less segregating groups of acini, none of them have been placed in this class if they showed any considerable amount of definitely encapsulated tumors. While these partially encapsulated groups of acini may represent definite growth centers, it seems quite as probable that their partial segregation may have occurred from irregular development of the stroma after the beginning of the pathologic process. The terms "adenomatoses" and irregularly diffuse colloid thyroid may properly be applied to them.

# A STUDY OF THE PATHOLOGY OF THE THYROID GLANDS FROM CASES OF TOXIC NON-EXOPHTHALMIC GOITER \*

LOUIS B. WILSON

## INTRODUCTION

That a secretion from the thyroid is the cause of the toxic symptoms in goiter has not yet been positively proved. Indeed, the proof is still somewhat incomplete that any secretion from the thyroid may be found in the circulating blood. However, evidence is slowly accumulating which it seems likely will ultimately prove both these propositions beyond peradventure.

Five years ago I gave a detailed analysis of the pathology of 259 thyroids removed from patients listed clinically as "exophthalmic goiter" in the Mayo Clinic from January 1, 1905, to May 10, 1908, and, in addition, a review of the pathologic reports of 35 cases similarly listed prior to January 1, 1908. I pointed out that above 76 per cent. of these glands showed primary parenchymatous hypertrophy and hyperplasia, and that, in general, the length and severity of the case-history could be predicated from a knowledge of the pathologic findings. The margin of above 20 per cent. of the patients on the "exophthalmic goiter" list whose thyroids did not show primary hypertrophy and hyperplasia of the parenchyma was explained at the time by the supposition that they were either "patients who have recovered from their toxic symptoms, and are now suffering principally from long, previously acquired heart and nerve lesions," or that they were "recently developed,

\* Presented before the State Medical Society, Minneapolis, Minnesota, October 2, 1913. Reprinted from *Amer. Jour. Med. Sci.*, March, 1914, and from the *Journal-Lancet*, February 15, 1914, pp. 93-97. Submitted for publication, October 29, 1913.

very mild or moderately mild cases of long standing." The fairly accurate estimates of the clinical condition from the pathologic data were made on the hypothesis that "the symptoms of Graves' disease are associated with increased absorption of an increased secretion of the thyroid." Since this report it has become possible more intelligently to interpret the pathologic pictures because of the increasing clearness of our conception of the various clinical types of goiter.

From an extensive and detailed study of all types of goiter Plummer has recently called attention to the fact that clinically there are two distinct groups of toxic goiters: one, exophthalmic and the other toxic non-exophthalmic. The former I have demonstrated pathologically all show primary hypertrophy and hyperplasia of the parenchyma as the dominant pathologic change in the thyroid. Allowing for a very small margin of error on both the part of the pathologist and of the clinician, all cases of clinically exophthalmic goiter coming to operation in the Mayo Clinic during the years 1911 and 1912 showed primary hypertrophy and hyperplasia of the parenchyma of the thyroid, and practically no cases of toxic non-exophthalmic or of non-toxic (*i. e.*, simple) goiter showed any such pathologic change.

Thus the evidence of the constant association of primary hypertrophy and hyperplasia of the thyroid with the symptoms of true exophthalmic goiter would seem to be fairly conclusive. Our previous communications have, however, touched but lightly on the pathology of the thyroid in cases of toxic non-exophthalmic goiter, and it is this phase of the subject to which I wish herein to call attention.

Plummer has shown that about 23 per cent. of all goiters reported as non-hyperplastic are of the toxic non-exophthalmic type, while the remainder are atoxic (simple) goiters. He notes further that "patients coming under observation with non-hyperplastic toxic goiter give a history of having first noticed the goiter at the average age of twenty-two years, and the evidence of intoxication at the average age of 36.5 years. The corresponding ages for hyperplastic goiter are respectively thirty-two and

32.9 years. That non-hyperplastic goiter is noted ten years earlier in life than hyperplastic goiter, and that 14.5 years elapse between the appearance of non-hyperplastic goiter and the development of notable toxic symptoms, while the constitutional symptoms are noted but a few months later than the goiter in patients affected with hyperplastic goiter, is alone sufficient to show that we are dealing with at least two distinct pathologic and clinical groups. That one is not the sequence of the other is self-evident."

Plummer further divides the intoxications from non-hyperplastic goiter into two merging groups: "(1) A group in which the cardiac toxin predominates and in which the clinical picture closely resembles, and in many instances cannot be differentiated from, the cardiovascular complex resulting from alcoholic, luetic, septic, and other well-known toxins; (2) a group more closely presenting the picture of Graves' disease, and including the cases that have been erroneously so diagnosed by the mass of the profession."

I wish to present in this paper the results of a somewhat intensive study of the thyroids from approximately equal numbers of cases taken consecutively in our series, the only selection being made consisting in the exclusion of cases of which full data were not at hand. This includes—(1) 431 thyroids removed from cases of true exophthalmic goiter during the years 1911 and 1912; (2) 373 thyroids removed from as many cases of non-toxic (*i. e.*, simple) goiter during the year 1912, and, (3) (a) 129 thyroids removed from toxic non-exophthalmic cases during the years 1910, 1911, and 1912, and clinically in Plummer's subgroup 2, *i. e.*, "cases with symptoms closely approaching the picture of Graves' disease," (b) 155 thyroids removed from toxic non-exophthalmic cases during 1911 and 1912, and clinically in Plummer's subgroup 1, *i. e.*, "cases in which the clinical picture closely resembles and, in many instances, cannot be differentiated from, the cardiovascular complex resulting from alcoholic, luetic, septic, and other well-known toxins," and (c) thyroids from 90 cases similar to the last, but of more mild or doubtful toxicity. The non-exophthal-



mic cases of clinical group 2 were included on the "exophthalmic goiter" list for 1910, 1911, and 1912, because of their resembling true exophthalmic goiter, while the cases of clinical group I were included on the "simple goiter" list because, though toxic, they did not resemble symptomatically the cases of true exophthalmic goiter. The thyroids from these cases have all been carefully analyzed as to their gross and microscopic pathology. A summary of the more important analytic data is presented in the following table:

#### DISCUSSION OF DATA

*Percentage Distribution.*—The distribution of the thyroids from each of the four clinical groups into the eight pathologic groups shows the following interesting points:

(1) Practically all the 431\* cases of true exophthalmic goiter show some stage of primary hypertrophy and hyperplasia; of the thyroids, 4 per cent. are in an early stage; 43 per cent. in an advanced stage, and 52 per cent. in a regressing stage. As I have previously pointed out, this regression may be due to—(a) the self-destruction of the parenchyma of the gland through the overfunctioning of hyperplastic tissue, or (b) the destruction of the parenchyma through surgical interference, *e. g.*, ligation of the thyroid arteries which had been performed in a large percentage of the cases in this series.

(2) Fifty per cent. of the thyroids from the toxic non-exophthalmic cases of clinical group 2 (*i. e.*, those which resemble more or less the true exophthalmic goiter cases) showed marked evidences of regeneration of the parenchyma (group D). I have elsewhere noted that regeneration of previously atrophic parenchyma of the thyroid is often a marked process, which can usually be differentiated from primary parenchymatous hypertrophy and hyperplasia by (a) the abundant presence of atrophic parenchyma within large acini; (b) the development of numerous new acini within one or more portions of the walls of the old, large, colloid-filled

\* These cases have been reported in detail elsewhere. See Wilson: Amer. Jour. Med. Sci., December, 1913.

COMPARISON OF PATHOLOGIC GROUPING OF THYROIDS FROM CASES OF EXOPHTHALMIC, TOXIC NON-EXOPHTHALMIC, AND ATOXIC (SIMPLE) GOITER

	PERCENTAGE DISTRIBUTION				AVERAGE AGE AT OPERATION				AVERAGE DURATION OF GOITER BEFORE OPERATION				AVERAGE WEIGHT OF PORTION OF GLAND REMOVED			
	374				374				374				374			
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Years	Years	Years	Years	Years	Years	Years	Years	Grams	Grams	Grams	Grams
A	4	..	..	..	25.0	..	..	..	0.3	..	..	..	88	..	..	..
B	43	..	..	..	31.7	..	..	..	0.9	..	..	..	61	..	..	..
C	52.5	..	..	..	40.7	..	..	..	3.5	..	..	..	51	..	..	..
D	99.5	..	..	..	35.9	..	..	..	2.3	..	..	..	55	..	..	..
E	..	50	17	9	..	34	32	38	..	6.9	15.3	8	..	100	153	143
F	..	12	7	10	..	39	47	39	..	4.4	5.8	13.6	..	97	139	122
G	..	33	14	18	..	43	50	48	..	12.6	22.7	24.2	..	91	186	129
H	..	45	21	28	..	41	48.9	44.7	..	8.8	18	30.5	..	83.7	102	172
	..	3	21	19	..	45	44	43	..	17.7	15.2	14.5	..	139	184	147
	..	2	41	44	..	52	46	41	..	12	30.2	16.5	..	140	196	164
	..	5	62	63	..	47.5	45	41.6	..	14	18.7	16	..	139	192	159
	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

acini, which early fill with dense colloid, and (c) the development of multiple layers of relatively small parenchyma cells within the large colloid-filled acini, which are distinguished from primary parenchymatous hypertrophy and hyperplasia by the smaller size of the parenchyma cells and the absence of papillæ.

3. Seventeen per cent. of the thyroids from the positively toxic cases in clinical group 1 (*i. e.*, those in which the clinical picture appears to be the result of a cardiac toxin) are of the regenerative (D) type. Though this percentage is but one-third that of the preceding group, it is still nearly twice that shown by the thyroids of doubtful toxicity and by the atoxic (simple) goiters, both of which gave the same (9 per cent.) in the regenerating (D) class.

4. Twelve per cent. of the thyroids from the toxic non-exophthalmic cases of clinical group 2 are early fetal adenomas, and 33 per cent. degenerating fetal adenomas, making 45 per cent. in all in which the pathology is that of encapsulated adenomas made up of acini of largely lumenless type. This leaves but 5 per cent. of the cases in clinical group 2 in which the pathology of the thyroid is that of colloid goiters with adult parenchyma. This is in strong contrast to the distribution of the thyroids in the toxic cases from clinical group 1, in the positive ones of which only 7 per cent. of the thyroids are early fetal adenomas, 14 per cent. degenerating fetal adenomas (21 per cent. in all), while 62 per cent. of the thyroids in this clinical group 1 are colloid goiters with adult parenchyma. This distribution is closely followed by the thyroids in the questionably toxic group—E, 10 per cent., F, 18 per cent., G, 19 per cent., and H, 44 per cent. respectively, which also is almost parallel with the distribution of the thyroids from the non-toxic (simple) goiters—E, 5 per cent., F, 18 per cent., G, 23 per cent., H, 44 per cent. This may all be summarized by saying that one-half of the thyroids from the toxic non-exophthalmic cases which more closely resemble true exophthalmic goiter (clinical group 2) are of the regenerative type, and nearly all the remainder are fetal adenomas, while in contrast to this only one-eighth of the thyroids from the toxic non-exophthalmic cases which do not resemble true exophthalmics (clinical group 1) are of the regenerative type,

less than one-fourth are fetal adenomas, and more than three-fifths of them are adenomas or colloid adenomatoses with adult and atrophying parenchyma.

*Average Age Distribution.*—Plummer has shown that patients with true exophthalmic goiter first notice the excessive development of the thyroid at an average age of thirty-two years, with evidence of intoxication developing 0.9 of a year later. The average age of these patients at the time of the removal of the thyroid was twenty-five years in those cases in which the parenchyma of the thyroid was found to be in an early stage of primary hypertrophy and hyperplasia (pathologic group A), 31.7 years in those cases in which it was in an advanced stage of primary parenchymatous hypertrophy and hyperplasia (pathologic group B), and 40.7 years in those cases in which it showed regressive changes secondary to primary hypertrophy and hyperplasia of the parenchyma (pathologic group C), or an average of 35.8 years for all cases in the group. The average age of the patient in clinical group 2 of the toxic goiter cases is lowest in those whose thyroids were of the regenerative type, and highest in those whose thyroids were colloid goiters with adenomas or adenomatosis. The same is true throughout the other two groups of toxic goiters. It is worthy of note that the average age of the patients with toxic symptoms in both clinical groups is considerably higher than the average age of the patients with non-toxic symptoms in each of the pathologic groups. This is capable of several interpretations, the more obvious of which are—(a) Regenerations of atrophic epithelium (group D) require considerable time for development of symptoms; (b) fetal adenomas on the average require more time for development, if ever, of toxic symptoms than do regenerations; (c) adult adenomas and diffuse adenomatoses are slowest of all types to develop, if ever, toxic symptoms. In general it may be said that patients with non-exophthalmic goiters either come to operation before they have developed their toxic symptoms at an average age of from thirty-one to forty years according to their pathologic classification, while patients with toxic non-exophthalmic goiters come to opera-

tion at an average age of from thirty-two to fifty-two years, according to their pathologic grouping. It is important, however, to control our deductions from a study of the average ages at operation by a consideration of the data of the next classification.

*Average Duration of Goiter Before Operation.*—The average duration of goiter before operation in the cases of true exophthalmic goiter is 0.3 year for those in which the thyroid was of pathologic group A (early primary parenchymatous hypertrophy and hyperplasia), 0.9 of a year in those of pathologic group B (advanced primary parenchymatous hypertrophy and hyperplasia), and 3.5 years in those of pathologic group C (regressing primary parenchymatous hypertrophy and hyperplasia). In the toxic cases of clinical group 2 the goiter had existed 6.9 years in those of pathologic group D (regenerations), 4.4 years in those of pathologic group E (early fetal adenomas), 12.6 years in those of pathologic group F (degenerating fetal adenomas), or an average of 8.8 years of the total fetal adenomas, and fourteen years in those in which the thyroids were of pathologic groups G and H (colloid goiters with adult parenchyma). When the first of these figures are compared with the average duration of the goiters in the other groups, it would appear that those cases in clinical group 2 (*i. e.*, toxic goiters resembling exophthalmics), though they develop later in life, as shown by the average ages at operation, yet are of sufficient intensity to bring the patients to operation considerably earlier than patients of clinical group 1 or those of the atoxic group.

*Average Weight of Portion of Gland Removed.*—The average weight of the portion of gland removed is in general a fair relative index of the total size of the thyroid. The examination of the averages of these weights for thyroids in the different groups shows that of those from cases of exophthalmic goiter, those in pathologic group A (early primary parenchymatous hypertrophy and hyperplasia) are the smallest,—38 grams,—those of pathologic group B (advanced primary parenchymatous hypertrophy and hyperplasia) are considerably larger,—61 grams,—and that those of pathologic group C (regressing primary parenchymatous hypertrophy and hyperplasia) are smaller than the preceding,—51

grams. In those from clinical group 2 (toxic non-exophthalmic), those of groups D and E are much smaller than those of any of the other groups—67 and 68 grams respectively. This observation is in harmony with the conclusions to be drawn from the average durations of goiter, since these relatively smaller glands are those not so much blocked with retained colloid as are the thyroids of the simple goiter type. Indeed, throughout this clinical group, the average weight of the glands of each of the pathologic groups is very much smaller than the average weight of the glands in parallel pathologic groups of either clinical group 1 or of that of the simple goiters.

#### GENERAL SUMMARY

1. The pathology of the thyroid in true exophthalmic goiter is essentially a primary parenchymatous hypertrophy and hyperplasia, *i. e.*, an increased amount of functioning parenchyma associated with an increased absorption. The process is an acute one.

2. The pathology of atoxic simple goiter is marked essentially by atrophic parenchyma, decreased function, and decreased absorption. The process is a chronic one.

3. The pathology of toxic non-exophthalmic goiter of clinical group 2 (*i. e.*, those resembling exophthalmic goiter) is one of increased parenchyma through regenerative processes in atrophic parenchyma, or the formation of new parenchyma of the fetal type, with an increase in each instance of secretory activity and of absorption. The process is a chronic one, but sufficiently active to cause the patient to consult a surgeon earlier than do those patients in clinical group 1.

4. The nearer the cases of clinical group 2 (toxic-non-exophthalmics) approach, in age and symptoms, true exophthalmic goiter, the shorter the duration of the period of goiter before operation, and the smaller the average weight of the gland at the time of its removal.

5. The cases of toxic goiter of clinical group 1 (*i. e.*, those in which the symptoms are of the cardiovascular variety) much more

closely resemble cases of simple goiter in their pathology in all respects than do the cases of clinical group 2. A larger number of them are of the colloid goiter type; the enlargement of the thyroid has existed for a longer period before operation, and the portion of the gland removed is materially larger than in those cases of clinical group 2.

6. Finally, it may be stated that all the above pathologic evidence points to a constant relative association of increased secretion and increased absorption from the thyroid proportional to the degree of toxicity on the part of the patient. We have as yet no absolute proof that such secretion and absorption is the cause of, rather than coördinate with, the symptoms, but the presented evidence strongly points to that conclusion.

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## SURGERY OF THE THYROID—OBSERVATIONS ON 5000 OPERATIONS \*

CHARLES H. MAYO

During the twenty-five years ending May 14, 1913, 5000 operations were performed on the thyroid in the clinic at St. Mary's Hospital. These operations were done on various types of goiters, and may be classified as follows:

Simple goiters . . . . .	2396
Including—	
Transplantations in cretins . . . . .	11
Operations for malignancy: carcinoma, 52; sarcoma, 7 . . . . .	59
Operations on syphilitic thyroids . . . . .	1
Exophthalmic goiters, including double and single ligation, extirpation, partial thyroidectomy . . . . .	2295
Early operations not classified, majority simple goiter . . . . .	309
Total† . . . . .	5000

An increase in the size of the thyroid may be physiologic or pathologic. In the higher invertebrates the gland has a marked sexual relationship, and through this association we have a suggestion that the thyroid may be a factor in the manifest disturbances which occur at certain periods, especially in the female, as the well-known goiter of adolescence, the congestion of the thyroid during menstruation, and its not infrequent enlargement during pregnancy.

While as yet we have no knowledge of a specific causative factor in the production of goiter, nevertheless a great deal has been learned during the past quarter of a century concerning the

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† Ten aberrant, one accessory, and one lingual thyroid are included in the total number.



physiology and pathology of the gland. Among its several functions the thyroid has been shown to be a *defense gland*, and that it has much to do with physical and mental development. It is evident that increased activity of the gland is required during infections in different organs of the body. Several observers, among them McCarrison, believe this demand to be occasioned by intestinal toxemia, and that this may play an important part is undoubtedly true. The work of various goiter commissions and the reports of those observers who have made a study of the etiology of goiter make it quite apparent that, whatever the agent, it seems to be more readily conveyed by water than by any other medium, although water is probably not the sole carrier. The so-called goitrogenous water, when boiled, is not infective. Evidence varies as regards intestinal toxemia. Boiled water contaminated with the feces of an individual having recently developed goiter has produced goiter in goats, while the filtered residue of goitrogenous water from districts in which goiters prevail has also produced the same result in man and the goat. This does not necessarily prove a specific agent; it may indicate a demand on the system for increased resistance and greater elimination of toxic material. Repeated tonsillitis is another disease in which an infection may have a bearing on the hyperactivity of the thyroid.

The thymus gland and the thyroid are undoubtedly intimately associated in the growth and development of early life. We now know that the thymus is much more regularly persistent throughout life than it was formerly supposed to be, and that not infrequently the gland may be of great size in advanced middle age, compressing the trachea at or just above its bifurcation. Such a complication is more common and more grave in late goiters of the serious hyperplastic type.

The occasional large goiter observed in the cretin has but little active parenchyma. If these goiters cause distress, they should be removed. We have repeatedly transplanted gland from the cretin's mother, and also from fresh simple and exophthalmic goiter. In none of these cases did the transplanted gland functionate, though for a short time it furnished secretion by absorption.

Changes in the voice are often caused by the presence of goiter. Large right-sided goiters quite frequently produce paresis of the left recurrent laryngeal nerve. It is, therefore, advisable to make a laryngoscopic examination before doing a thyroidectomy, which otherwise may be blamed for the paresis discovered later. Loss of voice through injury of the recurrent laryngeal nerve during operation is not a rare occurrence. Possibly 10 per cent. of patients have some temporary hoarseness, and about 5 per cent. a permanent difficulty with one cord, but without loss of voice. This percentage is small compared with the number of cases of paresis or paralysis due to the pressure of a goiter.

The left recurrent nerve, which is more frequently affected, lies slightly deeper than the right and has received more stretching during embryonic life. This may account in some measure for its greater susceptibility to injury from pressure. Extensive exposure of the nerve, as is done in some clinics, is necessary only in an operator's early experience, or in operating on nodular thyroids which extend beneath the trachea and which may have displaced the nerve. The scar tissue resulting from the traumatism of a too free exposure of a nerve may lead to secondary paresis.

Intrathoracic goiters and deep substernal goiters are of serious import and are found about once in 50 operations for simple goiter. Slight substernal projections are much more frequent. The diagnosis rests on—(1) dull area on percussion; (2) the roentgenogram; and (3) evidences of substernal pressure (dilated veins, obstructive dyspnea, and palpation of the upper pole or the gland just above the clavicle).

A special histology of the parathyroid glands was described by Sandstrom in 1880, and they have been the subject of much investigation and experimentation from a surgical point of view during the past few years.

While a great deal has been attributed erroneously to the parathyroids, they are worthy of serious consideration by the surgeon operating on the thyroid. There are four parathyroids in the human being normally, and, since the veins of these bodies have no valves, they are quite liable to imperfect development

through congestive conditions occurring during birth. Inasmuch as but one or two of them may be active and their injury during operation may cause tetany, their location must be avoided by preserving the posterior capsule, especially when both sides of the thyroid are operated on. Because of the difficulty in identifying the parathyroids, it is best also to preserve all small, gland-like bodies beneath or connected with the posterior capsule. Treatment, however, of operative tetany with calcium lactate and also beeves' parathyroid with thyroid extract has been very effectual. Our experience with this disease and treatment is limited to one mild case of temporary duration.

As regards the non-surgical treatment of goiter, there is no question but that many cases of simple goiter, especially of the adolescent type, undergo a natural resolution, which is also true of congestions and enlargements occasionally observed during pregnancy. In the hyperemic goiters of adolescence some form of iodine treatment may have a favorable effect. In encapsulated adenomas the use of iodine may manifest a temporary favorable effect on the surrounding gland, but the effect on the encapsulated tissue is uncertain. Its use between the ages of thirty-five and sixty seems to stimulate the activity of the thyroid and to cause degenerative changes. More recent experience in the non-surgical treatment seems to indicate the use of thymol, salol, and iodine as intestinal antiseptics. The administration of thyroid gland has rather an uncertain effect, yet apparently produces favorable results in the early treatment of simple goiters. In a considerable percentage of cases hyperthyroidism unquestionably is checked at various stages of the disease by natural or therapeutic measures. In exophthalmic goiters temporary improvement has been obtained by the use of the Roentgen ray, which seems also to be of value in carrying serious cases through exacerbations. The cytolytic serums for specific action on the thyroid have not borne out in their results the early expectations of the medical profession.

In operating on the thyroid the best exposure to be obtained is through a transverse incision low in the neck, the skin and platysma turned together each way from the incision. Should

further exposure be necessary, the sternohyoid may be sectioned high in the exposed area to prevent movement of the cutaneous scar and preserve a working muscle. In simple goiters it is best to extirpate a greatly enlarged lobe. If both lobes are symmetrically enlarged, division of the isthmus with double resection of the gland is indicated for the best cosmetic results. Midline encapsulated adenomas should be enucleated, with division of the isthmus. Lateral encapsulated adenomas may be enucleated or the whole lobe extirpated.

If symptoms of hyperthyroidism are present, extirpation is indicated. In severe cases of hyperthyroidism, in acute attacks and relapses or exacerbations, the condition should be considered medical until improvement takes place. If no improvement proves manifest under such care, injections of boiling water into the lobes (Porter) may give relief.

During the first three or four months of the symptoms extirpation can safely be made, since the heart then is not dilated. If dilated to exceed 1 inch, primary ligation of the superior thyroid vessels is indicated, followed in four months by extirpation. After the first year a much smaller percentage of cases requires primary ligation. A single test ligation on one side may be made in doubtful cases, to be followed in a week by a second ligation or partial extirpation, according to the degree of reaction.

The records of a large number of patients in this series show an average gain of 22 pounds within four months after ligation. These patients were then operated on, a partial thyroidectomy being done with safety. Following these methods of safety, we have performed 278 operations on cases of hyperthyroidism between deaths. Long-standing cases of simple goiter and adenoma may, by degeneration or chronic slow thyrotoxicosis, cause serious disturbances in the heart, kidneys, and blood-vessels. Especially is this true of patients in middle and advanced middle life. When such complications are present, operations are made with considerable risk.

Excluding malignancy, the mortality in operating on goiters is very low. It varies but little at present in the cases of so-called

simple goiter, in which class are included occasional complications, from the cases of so-called exophthalmic goiter with hyperplastic glands. In the early development of surgery, operations on exophthalmic goiters were delayed until serious complications arose with the heart, kidneys, or nervous system. This led to a high mortality, which naturally deterred physicians from sending patients to surgeons for early operation. The greater the delay, the greater the mortality—hence a surgical vicious circle. Our mortality in the first 16 cases (which were, of course, advanced) was 25 per cent.—about the average percentage in other clinics at that time. The mortality at present varies from 1 to 3 per cent. This great reduction in mortality is probably due less to operative skill and technic than to better judgment as to the time and extent of the operative procedure instituted, as well as to the skilled use and rational choice of an anesthetic. The various causes of mortality are hyperthyroidism, embolism, pneumonia, hemorrhage, sepsis, etc.

The results of operating on simple goiters are well known to be exceedingly satisfactory. Severe myxedema is but a rare complication following such operations, especially if the area of the gland nearest the capsule be preserved. The large colloid masses in the interior of these glands represent the great bulk of the tumor, but the least amount of the working area of thyroid tissue.

Operation in cases of hyperthyroidism appears to give about 75 per cent. of cures, while the remaining 25 per cent. are more or less benefited, according to the degree of complication and the stage of the disease. Probably 10 per cent. have some degree of relapse in from one to three years after operation, usually manifested by the return of symptoms. In these rare cases further operation by ligating the vessels, and in most cases by removal of a portion of the remaining lobe, improves the condition of the patient by reducing the amount of thyroid secretion. Exophthalmos of marked degree and long standing may still be present when other symptoms are cured. This is due to the gradual contraction of the non-striated muscle which sustains the globe to the anterior supporting orbital fascia (Sandstrom). In some cases we have

greatly improved this condition by removing the superior and middle sympathetic ganglions.

If the patient is in a good general condition without complicating conditions, a general anesthetic, for instance, ether by the drop method, is preferred. Ordinarily patients receive  $\frac{1}{8}$  grain of morphin and  $\frac{1}{150}$  grain of atropin half an hour before the operation. Nervous patients having exophthalmic goiter may receive  $\frac{1}{200}$  grain of scopolamin one hour before operation, but without the atropin, unless a general anesthetic is also to be given. Scopolamin is uncertain in its effects, some patients being made worse by its use. Patients suffering from grave complications rendering general anesthesia inadvisable can be carried through extensive operations by free local injections of novocain, 0.5 per cent.; and a combined local and general anesthesia, as advocated by Crile, may be of advantage in many cases. Intratracheal anesthesia is indicated in those cases of scabbard or distorted trachea in which the patient is already suffering from dyspnea, or more especially in those suffering from malignant disease of the thyroid, and complications due to enlarged thymus.

## A SUMMING UP OF THE GOITER QUESTION \*

CHARLES H. MAYO

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Concerning the development of the thyroid, embryologists have returned to their former belief that the gland is developed from a single instead of three anlagen. It originates between the three portions of the developing tongue, and early descends to its final resting-place upon the trachea. The tubular line of descent is known as the thyroglossal duct, and early undergoes obliteration. The remains of this structure often persist at the posterior portion of the tongue—the foramen cæcum. Gaskell has shown, however, that in the higher invertebrates the duct persists as such, and in great part delivers into the genital tract, the analogue of the thyroid thus being evidently a sex gland. Occasionally the gland remains in the tongue as a lingual thyroid, again portions are separated in descent as aberrant thyroids, or partially attached as accessory thyroids, while the midline cysts are usually due to the persistence of pharyngeal embryonic mucosa carried down in the thyroglossal duct by the descending gland.

The gland, horseshoe in shape and consisting of two lobes connected by an isthmus, rests astride the trachea, to which it is quite firmly attached by its capsule. No other organ in the human body is so well provided with a blood-supply. In proportion to its weight it receives 28 times as much blood as the head, and all the blood in the body passes through it, as it does through the brain, once every hour. It has been shown to be  $5\frac{1}{2}$  times more vascular than the kidney. While the lymphatics are numerous, those leaving the gland are small as compared with its wonderful

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blood-supply, apparent activity, and production of secretion. It is probable, however, that this secretion is delivered into the veins by short lymph-spaces throughout the gland itself. Baumann showed long ago that there was a high iodine content in the human thyroid. There is much less in herbivorous animals. Marine has done much work on the iodine-content of the thyroid in warm-blooded animals and fish. Hunt and Smith have carried on biochemical tests for the same substance.

The secretion of the thyroid is thin, watery, and non-stainable, and it is probable that the active cells represented by one-sixth of the gland are sufficient to furnish the necessary amount of secretion for the preservation of good health.

As has been stated, the gland in the higher invertebrates is apparently a sex organ. To some extent this relationship holds through vertebrates, including man. At the period of puberty some increase in the size of the gland is quite common. This is often noted during menstruation, and especially during pregnancy, while at the menopause many of the symptoms are apparently those of alternate hyper- and hypo-activity of the thyroid, as shown by its effect upon the nervous and circulatory systems and nutrition. While it is probably as active in the control of early growth, both mental and physical, as is the thymus, a child born without a thyroid fails to develop mentally or physically; and its loss in the adult usually leads to a peculiar deterioration known as myxedema.

The variations in the gland without symptoms are so great that it is almost impossible to state what is normal thyroid. Undoubtedly, the gland has a considerable storage function, and when this is carried to excess, it leads to local areas of stasis due to pressure-atrophy of the producing cells. Such glands constitute many of the atoxic (simple) goiters, though here also are included some of the encapsulated adenomas of both adult and fetal type. Colloid, then, may not be an essential secretion, but a spongy holding-material thrown out by the gland in exerting its storage function.

In exophthalmic goiter—so-called hyperthyroidism—there is



always a true hypertrophy and hyperplasia, an increase in the cells, and activity of the gland. Atoxic (simple) goiter includes about all varieties not inflammatory, exophthalmic or malignant, yet in this group have been included a large number of cases of toxic thyroid due to degeneration of the gland, and presenting many of the symptoms of exophthalmic goiter, particularly those of the cardiovascular system, but always without protruding eyes. These cases, in Europe, are frequently classed as pseudo-exophthalmic goiter.

In simple goiter there is the enlargement of the thyroid which may follow its normal contour, or occur in the isthmus or either lobe and present the colloid type. It may also be an encapsulated adenoma representing a rounded tumor of the whole gland or any portion of it. The sudden appearance of a tumor of the thyroid with symptoms of pressure may come from internal hemorrhage or from active hyperemia, while infections with severe, acute symptoms of toxemia are but rarely seen.

Substernal goiter is noted in about 1 in 40 cases of simple goiter; slight substernal projections occur much more frequently. They are diagnosed by symptoms of respiratory pressure, prominent veins extending from the neck to the chest, by percussion, and by the roentgenogram. The very large ones are, fortunately, of the encapsulated adenoma type, admitting of enucleation.

Simple goiters are subject to changes of the cystic type, especially the encapsulated adenomas, while fibrous and calcareous degenerations are seen, and some cases present all varieties.

Exophthalmic goiter presents a fairly sharp clinical picture. Its onset, as a rule, is relatively acute, and the course of the disease fairly definite. Early in the history the clinical picture is that of a toxin acting directly on the more vital organs, more notably the central nervous and vascular systems. Later, it is made more complex by the interaction of those organs whose functions have been directly disturbed by the toxin. "The order of onset of the more important symptoms, based on the average of our series, is as follows: (1) Cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia;

(6) loss of weight; (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice, and (13) death." In some cases certain of the symptoms may not be present in the early stages of the disease, which makes the condition difficult to diagnose. There are certain conditions of the nervous system of unknown origin which much resemble this disease. As a rule, however, these patients have symptoms extending over many months. They have neither exophthalmos nor an increase in the size or density of the gland, and are not benefited by operation on the gland.

In carcinoma and sarcoma of the thyroid the picture is usually one of rapid growth of the gland, which becomes hard and irregular, often with neighboring glandular involvement. These symptoms may also occur in a simple goiter of long standing. Because of lymphatic and venous delivery with the early capillary involvement, early metastases in glands and lungs are common, and local recurrence is the rule. In such cases, when the disease is confined within the capsule, treatment requires removal of the entire gland.

Because of their interrelationship in function and location the parathyroids and the thymus are considered in relation to the diseases, and especially to the surgery of the thyroid. The parathyroids are usually four in number—a superior pair and an inferior pair. They are situated on each side and behind the thyroid, but intimately connected with its capsule. Much is attributed to the action of these little bodies in maintaining the equilibrium of the mineral salts of the body, especially of the calcium. Experimental evidence shows that, when removed from animals, a condition of muscular spasm, known as tetany, develops following a rapid loss of the mineral salts. The blood-supply consists of terminal branches from the vascular anastomosis between the inferior and superior thyroid arteries. Their veins have no valves. Thus they frequently become injured by hemorrhage during the congestion occurring at birth, to which are attributed infantile tetany and also tetanic attacks of later childhood and even of adult life. Tetany following operation is ap-

parently associated with their removal or an injury to their blood-supply, associated with a great loss of thyroid tissue. In such cases the best treatment is the feeding of beeves fresh parathyroids, and, following MacCallum's plan, the restoration of calcium to the body, preferably through the administration of calcium lactate in 5 per cent. solution, at repeated intervals. In addition to this the feeding of thyroid is indicated, and some cases are reported as benefited by the parathyroid serum.

Some investigators maintain that the thymus and thyroid are interrelated in influencing the growth of the body, and state that in the hyperplasia of the thyroid the thymus is usually found enlarged. While coexisting enlargement of the thymus with the goiter is present in many cases, yet it by no means holds good in some of the more serious ones, as shown at autopsy following both medical and surgical deaths of these individuals.

The thyroid consists of a number of groups of cells, which may be found even in the adult in various stages of development, from unarranged embryonic cells—Wölfler's rests—to well-developed follicles lined with epithelium, secreting into a well-marked central cavity. The simplest change is hyperemia, which may be temporary, occurring through the nervous system or more prolonged through systemic infections. It may be sufficient, however, to produce hemorrhage within the gland.

Acute inflammation of the thyroid may occur as the result of traumatism or general bacterial disease. Progressive hyperplasia consists in an increase in the number of parenchymatous cells, usually of a hypertrophic type, either in single or multiple layers. This may occur in parts of the gland or throughout all of it. True adenomas of the thyroid can be identified only when encapsulated. Histologically, they are either fetal adenomas, the parenchyma of the true fetal type, or adult adenomas, in which the parenchyma has taken on adult characteristics, *i. e.*, follicles lined with cells of adult type and subject to all the changes which are noted in the thyroid outside of encapsulated tumors, that is, the various degenerations.

Of the retrogressive changes, retention of secretion is the more common the simpler and more nearly the normal physiologic state,

as the thyroid is not only an actively secreting organ, but has, normally, a storage function. Colloid appears to be the basis for the preservation of this secretion. When it occurs in excess, the condition is pathologic, and leads to degeneration or atrophy of cells.

Atrophy of the thyroid results from overwork, pressure, and lack of nutrition to the gland. Simple goiter may undergo such a degeneration from these causes, and in the production of toxic materials so affect the circulatory and nervous systems that the condition resembles the more severe toxic state of exophthalmic goiter, or, in fact, any chronic toxemia.

To a variable degree thyroid enlargement may be due to demands made upon its secretion by certain systemic conditions, such as sexual development at puberty, the goiter of adolescence, the enlargement or hyperemia at menstruation, enlargement in the latter part of pregnancy, the changes at the menopause, and last, but not least, the possible iodine demand occasioned by bacterial infection of various organs.

Accumulated evidence shows that endemic goiter frequently comes from a water-borne irritant. In such cases ensuing chronic intestinal toxemia may occasion the extra demand on the thyroid. McCarrison, in his investigations of the subject in India, has done much to prove this.

The various types of goiter should be treated both medically and surgically. Many goiters of the simple and mild exophthalmic type undoubtedly recur spontaneously, although various forms of medical treatment may hasten the recovery and restoration of the gland to an apparently normal condition in many instances, especially in the early stages of simple goiter.

Simple colloid goiter which has resisted treatment and encapsulated adenomas are in most instances best treated by removal of the diseased portion of the gland, with preservation of its better portions. If the diseased part is not removed, such glands will, later in life, expose the individual to a serious menace, since the degeneration which follows in an average time of about fourteen years may be of such a character as permanently to damage the heart, kidneys, and liver. During middle life such degeneration

frequently follows the ill-advised use of iodine; the severity of the toxic process places these patients on a par with the severe types of exophthalmic goiter. Plummer has shown a great similarity in the damage to the essential organs of the body, such as the heart, kidney, and liver by various forms of toxemia. In exophthalmic goiter, however, the essential condition identifying it from all other toxemias is the parenchymatous increase of the thyroid. Exophthalmos occurs in no other systemic condition. The staring eye (Stellwag) and the widening of the palpebral fissure (Dalrymple) may occur with other toxic myocardial lesions, especially that of advanced Bright's disease. Exophthalmic goiter is essentially a disease of a chronic character, presenting exacerbations and ameliorations of symptoms extending over a period of months or several years. After the first year the gland often undergoes a regression.

While this disease is amenable to surgical treatment by the removal of a large amount of the hypersecreting gland, it is by no means emergent surgery, and all patients, during periods of exacerbation, should be considered as medical cases. Surgery is indicated in the up-wave of improvement. The majority of these patients can withstand thyroidectomy at the time they are seen by the surgeon. Extreme conditions, especially dilatation of the heart, may require medical preparation, and the operative interference following in cases resistant to treatment should be confined to injections of boiling water into the gland after Porter's plan to hasten improvement. In most of the severe cases a ligation is made first of the left upper pole only. Should the reaction following this be severe, the ligation of the right upper pole is indicated a week later, and thyroidectomy reserved until four months have elapsed, by which time these patients have made an average gain of 22 pounds, with great general improvement. However, if the reaction following the left ligation is not unduly severe, a partial thyroidectomy may be made at the second operation the week following.

In operating, the best exposure of the thyroid is obtained by a curved transverse incision through skin and platysma, extending between the anterior jugular veins, with wide separation of the

flaps, and midline vertical division of the muscles exposing the thyroid. If division of the muscle be necessary, it should be made at the upper part of the dissection, to break the line of scar and preserve muscle-function. In some cases the wound may be closed without drainage, the cavity being filled with salt solution. As a rule, however, patients having tubular drainage for twenty-four hours are more comfortable. A subcuticular closure of the wound with catgut, approximating first the platysma muscle, secures almost an imperceptible scar.

The anesthetic of choice in most instances is ether. Complicated cases, however, may be best carried through the operation by the local use of 0.5 per cent. novocain solution, with the addition of a little adrenalin. Occasionally the combined use of a local with a general anesthetic is advisable, a method which Crile has done much to popularize; the local anesthetic relieving the pain necessitates less of the general anesthetic to secure sleep.

In severe forms of Graves' disease the use of  $\frac{1}{200}$  grain of scopolamin with  $\frac{1}{6}$  grain of morphin one hour previous to operation is often a distinct advantage. Some patients seem to have an idiosyncrasy to the drug, and in such cases the operation must be postponed twenty-four hours to permit elimination. In all cases in which ether is used as the general anesthetic  $\frac{1}{100}$  grain of atropin should be given one-half hour before the operation, to maintain a dry trachea and pharynx during the operative procedure.

The great lowering of mortality following operation for exophthalmic goiter is due less to trivial details of technic than to the better judgment in the preparation of patients, the selection of a time, type, and extent of operation, and its division into stages, with varying intervals of rest.

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# A SUMMARY OF THE RESULTS OF RECENT INVESTIGATIONS OF THE THYROID IN RELATION TO SYMPTOMA- TIC GOITER \*

LOUIS B. WILSON

The belief that we have recently reached some degree of certainty in several phases of the investigation of the problems relating to the physiology and pathology of the thyroid, accompanied by the knowledge that we are still far from a complete solution of these problems, leads me to summarize briefly the present situation and to venture certain suggestions for further investigations.

## ANATOMY

1. The thyroid is a congeries of unconnected acini, each of which is capable of taking on changes different from those in adjoining acini. Only general causes can affect such a gland equally throughout.

2. Direct communication between the lymphatics and the blood vascular system of the thyroid has been demonstrated in elasmobranchs by Ferguson. Sistrunk, in the laboratories of the Mayo Clinic, has made a painstaking attempt to demonstrate a similar condition in the human thyroid by methods of injection. His work as yet remains indeterminate, because of the extreme difficulty in the technic. The solution of this problem may furnish the reason for the occasional apparently rapid absorption of the thyroid secretion, though if such a secretion passes into the

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lymphatics at all, it must ultimately reach the blood-stream by way of the thoracic duct.

#### EMBRYOLOGY

3. It is now fairly determined that the human thyroid develops from a single bud from the center of the ridge between the first and second ventral pharyngeal grooves. Grosser shows that the buds arising laterally and forming the ultimobranchial bodies have nothing to do with the formation of the thyroid in the human species.

4. Gaskell, in a detailed study of much new material, has reviewed the relationship of the endostyle in *ammocetes*, the larval form of the lamprey, to the similarly placed sex-gland in *homarus*, and presents convincing evidence that the two are homologous. He is sure that in *ammocetes* the endostyle does not functionate as a slime gland for entrapping food-particles, as formerly has been believed. He suggests that in *ammocetes* the gland may still have a definite sexual relationship.

5. Marine has studied in detail the metamorphosis of the large embryonic thyroid endostyle of *ammocetes* into the small, ductless thyroid of the adult lamprey. He shows that of the five varieties of epithelium found in the open organ of the larva, one or two persist in the ductless gland of the adult.

#### PHYSIOLOGY

While we have long known that there is a secretion in the thyroid, as yet we do not know positively that all or any portion of this secretion as such finds its way into the circulation. Aside from the facts that the secretion appears to be absorbable and that it may disappear from the gland, the following observations point to the inference that it is absorbed:

6. Hunt's acetonitril test for iodine, in the hands of Smith, is suggestive, though but slightly so, of the presence of an iodine-containing compound derived from the thyroid and circulating in the blood.



7. The work of Blackford and Sanford, suggested by the experiments of Gley, show that the same depressant action on the dog's blood-pressure may be obtained by injecting dogs with serum from patients with active exophthalmic goiter, as is obtained by injecting dogs with fresh extract of thyroid from similar cases. What is more important, they have further shown that when once a tolerance has been established by one or two injections of the depressor substance from either source, a tolerance also exists to subsequent injections of the depressor substance from the other source, and that this tolerance does not hold against subsequent injections of any of a number of more or less depressant substances derived from other sources. If these observations of crossed tolerance are confirmed, they would seem to establish the presence of similar, though not necessarily identical, substances in the thyroid and in the blood-stream of patients with acute exophthalmic goiter.

8. Blackford's and Sanford's experiments in connection with Smith's determination of the iodine content of the thyroid show that the proportion of cardiac depressant in the human thyroid is in inverse ratio to the amount of iodine per gram weight of the gland.

9. Marine has shown that he can induce hyperplasia of the thyroid in fish and in other lower animals by giving certain foods, *e. g.*, liver, and that there is regression in the thyroids of these animals when the special feeding is stopped, and when iodine is administered in small quantities.

10. Halsted, in a recent attempt, has failed to repeat his classic experiments on the production of a compensatory hyperplasia in the remaining portion of the dog's thyroid after a partial thyroidectomy, and now thinks that his former results were due to some infection or error in technic.

11. McCarrison, in an elaborate series of experiments, has succeeded in producing simple goiter, not only in man, but in several of the lower animals, by the administration of "goiterous" waters, of filtrates from the same, and of pure waters contaminated with feces of goiterous animals.

## PATHOLOGY

12. I have shown that: (a) In patients clinically in an early stage of exophthalmic goiter the thyroid glands show an early stage of hypertrophy (increase in size) and of hyperplasia (increase in number) of the parenchymal cells, with an increased amount of secretion, which is correspondingly reduced in density and increased in absorbability; (b) that in patients clinically in an active, advanced stage of exophthalmic goiter, the pathologic changes noted in (a) are correspondingly active and advanced; and (c) that in patients in whom the clinical symptoms of exophthalmic goiter are regressing the pathologic changes in the gland show corresponding regression and inversion of the pathologic processes noted in (a).

13. I have shown that in patients diagnosed clinically as simple goiter, or, better, as goiter with only pressure-symptoms, the thyroid does not show the changes noted in 11 (a), but that, on the contrary, it does show thinned atrophic parenchyma and an increased amount of a secretion which has an increased density and a decreased absorbability. I have not found any evidence in these cases to support Marine's hypothesis, based largely on animal experiments, that diffuse goiter is always secondary to a stage of parenchymatous hyperplasia. Neither is Marine's hypothesis in consonance with the clinical observation that cases of exophthalmic goiter (with which we have found hyperplasia constantly associated) are usually rare in regions where simple goiter is endemic in man.

14. I have shown that in patients which were formerly designated clinically as "exophthalmic goiter of mild continuous type," but which have been more recently differentiated clinically by Plummer as "toxic non-exophthalmic goiter" of chronic development, the thyroid does not show the changes noted in glands from cases of exophthalmic goiter, nor the diffuse colloid changes which preponderate in glands from cases of simple goiter, but that there are present in half the cases encapsulated adenomas, and in most

of the remainder evidence of regeneration of previously atrophic parenchyma.

While the relationship thus established, as noted in paragraphs 12, 13, and 14, between the histopathology of the thyroid and the symptoms associated with a gross enlargement of the gland, is best explained on the hypothesis that the apparently toxic symptoms are due to the absorption of a secretion from the gland, it must be conceded that this relationship, if considered alone, is explicable also on the hypothesis that the clinical and pathologic conditions are both the result of some other process wholly extraneous to the thyroid, and that the parallelism of the clinical and pathologic changes is but the result of this hypothetic general process.

#### CLINICAL DIAGNOSIS

15. Plummer has demonstrated that there are at least three distinct symptom-complexes associated with thyroid enlargement: (A) Typical exophthalmic goiter; (B) toxic non-exophthalmic goiter, and (C) atoxic or simple goiter. He has shown that these symptom-complexes are apparently distinct entities, as is indicated by—(a) The time of onset; (b) the difference in the order of their development, and (c) the difference in the symptoms. He has further shown that true exophthalmic goiter pursues a fairly definite order of onset of symptoms, with regular development to a point at which a sudden remission may be expected, and that wholly irrespective of treatment. Plummer points out that this phase of a drop in the clinical curve of exophthalmic goiter occurring at a definite period, which is analogous to the crisis usual on the eighth day of pneumonia, tends to cast doubt on the value of the apparent good results from either medical or surgical treatment of exophthalmic goiter. Thus the use of such results as proof of the relationship of hyperfunction of the gland to the clinical symptoms is also weakened. Conclusions drawn from tabulations of the results of treatment in any series of cases in which this factor is not considered must contain a large element of error, but, as Plummer points out, if the definite normal course of

the disease is recognized, then it becomes no more a disturbing element in the interpretation of the results of treatment than is the crisis in the interpretation of the results of treatment in pneumonia.

#### FURTHER STUDY

16. While the theory that changes in the thyroid gland are responsible for the clinical symptoms of exophthalmic goiter and of toxic non-exophthalmic goiter is supported by much the largest weight of evidence yet submitted, still it cannot be considered absolutely proved. I believe, however, that the theory may be susceptible of absolute proof along the following lines: (A) The production of symptoms in susceptible animals by injections of fresh extract from the thyroid, a field which by no means has been completely covered negatively; (B) by the production of symptoms in susceptible animals by the injection of chemical derivatives of the thyroid; (C) by showing that in the blood of exophthalmic goiter patients there exists a substance derived from the thyroid; (D) by showing that the removal of the thyroid in a large number of exophthalmic goiter patients at a time when the normal drop in their clinical symptoms could not be expected was associated with permanent recovery from the symptoms.

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## HEAD, TRUNK, AND EXTREMITIES





## MIKULICZ'S DISEASE\*

CARL FISHER

---

The so-called Mikulicz's disease has been appropriated by ophthalmologists to some degree because of the frequent involvement of the lacrimal glands. The disease is rare enough to warrant the report of a single case, especially as striking as this one. The following history may serve as an example of a typical case. The accompanying photograph (Fig. 264) is an unusually vivid one.

*Case Report.*—J. A., male, aged forty-seven, married, ranch laborer. *Examination* August 15, 1913. *Previous history* not important. Uses alcohol and tobacco. Neisserian infection twelve years ago. *Present condition:* He complains chiefly of swellings of the face, mouth, and lids. *Clinical history:* Five years ago swelling appeared under the lower jaw; six months later under the right jaw; eighteen months ago over the eyes, and six months ago in the axilla and groins. The swellings have never been red nor painful. His voice for three years has been somewhat husky. For past two years slight difficulty in breathing; no dysphagia. The swellings have increased in size slowly and progressively to the present time. He sleeps a great deal, and for the last six months has done no work on account of general weakness. He has some slight dryness of the mouth lately, but no insufficiency of tear production.

*Physical Examination.*—Normal weight, 205 pounds; at present, 170. This loss of weight said to have occurred during the last year. The lacrimals and accessory lacrimals, sublinguals, submaxillary, and parotid glands are all greatly enlarged, the enlargement being symmetric. The tumors are smoothly rounded, somewhat elastic, not fluctuating and not inflammatory. The

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tonsils are greatly enlarged. On account of the enlargement of the lacrimal and accessory glands, the lids show considerable ptosis, and the eyeballs are somewhat pushed forward, though their motion is unimpaired. The groins and axillæ present glandular enlargements the size of small beans. Chest and abdomen apparently perfectly normal, except for enlargement of the heart. The x-ray, however, shows considerable mediastinal thickening. The examination of the ears shows the drums much retracted,



Fig. 264.—Case A90111. Mikulicz's disease.

probably from pressure on the Eustachian tube. The turbinates are considerably engorged, eye-grounds and reflexes normal.

*Blood Examination.*—Hemoglobin, 69 per cent.; reds, 4,200,000; number of leukocytes, 8200, of which small lymphocytes, 16.3 per cent.; large lymphocytes, 4 per cent.; polymorphonuclears, 79.3 per cent.; eosinophiles, 3 per cent. Very slight variation in the size of the red cells. Specimens were taken from the sub-maxillary region, and the lacrimal glands were entirely removed for diagnostic purposes.

*Microscopic Examination.*—The tumor consists almost entirely

of lymphoid cells of rather large size. These show a moderate increase of mitotic figures. The tissue does not show any definite arrangement, though here and there are found septa of connective tissue, and in one or two places apparent formation of new connective tissue, with an occasional fibroblast. No remnants of glandular tissue or ducts are visible in any part of the tumor, although the tumor comprises the whole of what was the gland, being inclosed in the old glandular capsule. No eosinophiles or chronic inflammatory cells are present. The blood-vessels are fairly numerous, and do not show any significant changes. Staining for bacteria gives a negative result.

The racemose glands of the mouth and the lacrimals may be regarded pathologically as composed of two distinct elements: the glandular and the lymphatic structures proper. The lymphatic tissue corresponds in structure to the lymphatic nodes elsewhere in the body, and is scattered throughout the interstices of the lobules of the gland. Either element may become involved in a pathologic process independently of the other. Mikulicz's disease is primarily an affection of the lymphatic elements, the change in the glandular portion being purely secondary, and this probably entirely due to mechanical factors, *e. g.*, cutting off blood-supply, obstruction to the secretory ducts, and pressure-degeneration of the gland epithelium.

Clinically, a typical case of the disease is characterized by a symmetric, smooth, somewhat elastic enlargement of the salivary or lacrimal glands. This may involve any of the pairs of glands separately or in combination with other pairs. In this case all the glands were involved, even the tonsils apparently sharing in the process. The disease runs a chronic, benign, non-inflammatory course, with occasional fluctuations in the size of the swelling. The symptoms depend largely on the amount of pressure exerted by the tumor. When this makes respiration or deglutition difficult, the general health may be considerably affected. The destruction of glandular tissue may give rise to a dry mouth or a diminished secretion of tears. The blood count in a typical case is normal. The disease is self-limited, the growth becoming increasingly rich in connective tissue until the other elements are de-

stroyed. Sex is not a factor; it is in general a disease of middle age (Lintz gives the age limit as between four and seventy).

Microscopically, the findings of various observers have not been entirely in accord. The larger number reported have corresponded to Mikulicz's description,—as does our case,—namely, a pure lymphomatosis. Minelli's view of the process does not seem to me to have been seriously affected by the findings of others, and his case represents the other type commonly found. This consists primarily of a proliferation of the lymphatic cells already present in the gland, the gradual substitution of this lymphomatous tissue by connective tissue, and the mechanical destruction of the glandular structures. The destruction of tissue gives rise to cysts and foreign-body giant-cells, which are found fairly plentifully in the region of the destroyed epithelium. He reports large numbers of eosinophiles, cells which he considers fibroblasts, and many mitotic figures in the lymphatic cells. Wallenfang and others report endothelioid cells. The view that the degeneration of the glandular epithelium is primary and independent of the lymphatic hyperplasia has little support.

The most interesting aspect of this disease, and the most provocative of dispute, is the question as to its right to be called a pathologic entity. This involves a complete exposition of the whole question of lymphatic hyperplasias, a subject of which our knowledge is at present in a nebulous state. Warthin believes that all lymphoid hyperplasias are genetically related. They may be divided into—(a) leukemic and (b) aleukemic hyperplasias. There is no fundamental difference in the pathology, and one may pass into the other.

The findings in Mikulicz's disease have either resembled closely the picture of Hodgkin's disease or of pure lymphoma, so that the relation of Mikulicz's disease to this group is at least very close, if it does not amount to identity. Furthermore, though it is exceptional, cases called Mikulicz's disease have been reported in which a general lymphatic enlargement has later developed. In our case it seems likely that the mediastinal glands were sharing in the process, as well as the tonsils. The axillary and inguinal

glands were so slightly enlarged as to seem not diseased. Warthin found that lymphatic leukemia developed in two cases of symmetric enlargement of the lacrimal glands which he had regarded as regional lymphomas. On the other hand, both leukemic and aleukemic disease may involve the parotids or lacrimals. Furthermore, hyperplasias of lymphatic tissues confined to other regional systems are well known. In fact, a continuous series may be demonstrated of all combinations, from isolated swellings of the lacrimal glands to general pseudoleukemia (Wallenfang), and, it might be added, lymphatic leukemia.

The evidence seems conclusive that the term Mikulicz's disease should be regarded as one of convenience, like the term Hodgkin's, and not be understood to denote a real pathologic entity. The final determination of the ultimate nature of the disease must await the solution of the general problem of lymphatic hyperplasias.

The etiology likewise remains unknown. The organism of Hodgkin's disease, recently described by Bunting, may prove to be the solution; but this remains to be worked out. A host of theories have been advanced as to the etiology. None has been proved.

*Treatment.*—The future offers a prospect of successful treatment by serum therapy, if Bunting's work proves successful, as it has in some cases of Hodgkin's disease. Meanwhile potassium iodid, mercury, arsenic, radium, and Roentgen rays hold the field. I have seen several cases of bilateral parotid enlargement of unknown origin subside under potassium iodid and mercury, as is sometimes the case in Hodgkin's disease. Simple excision of the glands will relieve symptoms of pressure, and once excised, the growth will not return.

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## EPITHELIOMA OF THE EXTERNAL EAR\*

CARL FISHER

---

I have chosen to investigate the subject of epithelioma of the external ear exclusive of the middle ear, because the latter is always fatal, and is usually secondary to epithelioma of the canal or auricle, and hence middle-ear cancer is of rather academic interest.

Some idea of the infrequency of epithelioma of the external ear may be gained from the following:

West states that in ten years at the London Hospital there were 30 cases of malignant diseases of the pinna among 200,000 patients a year. In two years at St. Bartholomew's Hospital there were 7 cases. McBride reports having seen but 3 cases in twenty years' practice. There were 2 epitheliomas of the pinna in ten years at the Liverpool Eye and Ear Hospital. Accordingly, it may not be amiss to record the 27 cases observed in the Mayo Clinic from December 31, 1907, to October 31, 1913. In addition to this I have collected 22 cases more or less completely reported in the journals. The data on our cases are fairly complete, with the exception of the final results, which, in some cases, are in doubt either because the patients did not reply to letters sent them or because a long enough time has not elapsed since they were dismissed, apparently cured. Most of the cases in the literature examined are incompletely reported, especially as regards prognosis. No cases were considered where a report of the microscopic findings was lacking.

Anatomically, there are several features of the external ear which bear on the subject. The pinna is prominent enough to be

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the object of fairly frequent injury. The auriculomastoid furrow is frequently irritated by eczema and the bows of spectacles. The canal, concha, and lobe are exposed to the irritating discharges of middle-ear suppuration. In addition, the canal is exposed to hardened wax and much manipulation. The skin of the external ear is well supplied with large sebaceous follicles, the origin of all rodent ulcers, according to Bland-Sutton. Underlying the skin closely is the cartilage, which forms a barrier to the spread of epitheliomas, as well as a protection to them once the cartilage is invaded. The lymphatic drains are divided into three groups:

I. The posterior group, draining part of the external surface of the pinna, all the internal surface, and the posterior walls of the external auditory canal.

II. Inferior group, draining lobule and adjacent parts of pinna and inferior wall of external auditory canal.

III. Anterior group, draining trunks from the anterior part of the external auditory canal and concha, leading to the parotid glands and a node in front of the tragus.

Of these patients, the average age of incidence was sixty-two years; the youngest was forty-six. The youngest age I find reported was a case of epithelioma of the canal in a boy of eighteen. Males greatly predominate—74 per cent. of our cases to 85 per cent. in the literature. This is probably due to the greater exposure to injury of weather and trauma in the male.

In 71 per cent. of our cases the epitheliomas were primary in the pinna, though several had spread to the canal when seen. No point of origin greatly predominated, though the auriculomastoid fold and the region of the meatus were perhaps the more common.

As regards etiology, it happens that none of the epitheliomas of the canal were caused by chronic suppuration, though writers generally give this cause the most prominent place. Two of our cases had a preceding eczema of the canal and one a history of hardened wax. Two had a history of furunculosis of the canal, which was found to be cancer on microscopic examination. Of those primary in the pinna, injury was the most prominent cause given. Eczema of the auriculomastoid furrow and what seemed

to be sebaceous cysts were also common. In most of the cases the skin was of the type which seems ready to blossom forth into cancer on slight provocation—often small areas of keratosis were found about the face and neck—the so-called “sailor’s skin,” most often seen in people of blonde complexion who burn easily in the sun and wind.

These epitheliomas may be divided into the squamous-cell variety, originating in the corium, and the rodent ulcer or basal cell, originating in the sebaceous follicles. Pathologically, these distinctions are not clear-cut. All these tumors show cells of both the squamous and basal-cell type, and the difference seems to be chiefly a clinical one, especially in late cases. The origin of rodent ulcers in sebaceous follicles is questioned by many pathologists. The somewhat artificial distinction, however, is convenient. Clinically, the squamous-cell type predominated slightly in this series, though the prognosis was practically the same. This is also true of the cases reported in the literature, squamous type considerably predominating. Nearly all were of slow growth, the average duration before coming to examination being six months, though cases of four and twelve years’ standing were not uncommon. One case was said to be of twenty-three years’ standing, and Braislin mentions two cases of thirty-five years’ standing.

In spite of the long duration, glandular involvement was found in but four cases. A larger percentage (40) was found in the literature. The cases here were all of the cervical glands, the general experience being that the preauricular and the cervical glands are most commonly involved, simply foreshadowing the location of the growth. Of those having glandular involvement, the average duration before coming to examination was four years. Three-fourths of this group were primary in the pinna, both in our series and in the literature studied. None of these cases were classified as rodent ulcers.

*Diagnosis.*—This is usually obvious enough, but, nevertheless, the number of mistakes made clinically is rather striking. Two of our cases were called furunculosis of the canal until the progress



of the disease and the age of the patient suggested the necessity of microscopic examination. In the literature I find many cases mistakenly called granuloma of the canal, which later proved malignant. Beginning "rodent ulcers" before they became ulcerative were often called warts or sebaceous cysts until the growth aroused suspicion. Chancres, gummas, and lupus are usually given as likely to simulate cancer; in practice, this differentiation has not proved difficult. It is always easy to excise specimens for examination, but in the superficial indolent growths of small size, where radium or simple actual cautery may well be used, treatment should follow immediately the taking of a specimen rather than allow the stimulated tumor to grow. Pain is often quite a prominent symptom in canal cases; it is more severe than in ordinary furunculosis or suppuration in the middle ear. Many cancers gave rise to a discharge of blood and fetid matter where no middle-ear suppuration was present. Chronic canal disease in people over sixty years of age should always be examined with malignancy in mind. Primary cancer of the pinna was not found to occur in young people. It may, however, occur in the canal of young patients because of the irritation of middle-ear suppuration. It must be emphasized, however, that in cases of doubt microscopic examination should never be omitted, for on this, after all, the diagnosis must rest.

*Recurrences.*—I find the data in the literature very meager on this subject. Of the present series (considering only those without glandular involvement), 58 per cent. recurred. Note that this does not refer to final cures, which will be mentioned under Prognosis. Most of these recurrences were small nodules at the site of operation, and were easily cauterized away. In no case were there recurrences in the glands where these were not involved previously. The average time of recurrence is two months, four months being the longest. Considering, in addition to the ones who answered or were seen some time after operation, those whose prognosis was registered in the histories as "not likely to recur" (this based on the superficial character of the growth or the clinical course under observation), 50 per cent. did not recur at any

time. Of the cases which did recur, it is noticeable that all were adherent to the cartilage; all were primary of the pinna—this last probably depending on the greater tendency of rodent ulcer to attack the pinna. There is no doubt that the thoroughness of the operation performed is a most important factor, granting that the case is legitimately operable. In many cases the operation was doubtless less radical than it might have been, because of the desire to do as little mutilation as possible, the feeling being that if the patient can be watched, a small nodule or two may be easily removed.

*Treatment.*—Actual cautery or radical local excision and cautery has been the treatment followed in most of the cases. It is in general by far the most effective treatment for epitheliomas in this region. I cannot find enough accurate data in the literature to make a statistical comparison between this method of treatment and simple excision, radium, pastes, or x-ray. Few patients come to us without a history of treatment with ointments, pastes, or Roentgen-ray. Still, there is no doubt that pastes persisted in and skilfully used are effective in selected cases, as witnessed by one case of excision and cautery in our clinic which recurred but was cured by a paste treatment which also removed the whole of the external ear. The objection to caustic paste lies not so much in the method, but in its terrible abuse by all manner of quacks who do not dare attempt anything surgical, and jump at this means of keeping the patient among their sources of revenue.

The Roentgen-ray, while undoubtedly occasionally successful, is not to be depended on, and should not be used save as an after-treatment unless the patient can be under close supervision until cured. Its use is best confined to superficial, slow-growing epitheliomas.

In our hands radium has been more effective on the whole than the Roentgen-ray; its use should be confined to the same class of cases. In adherent or deeply seated growths, however, it is ineffective, and, like all ineffective methods in the treatment of cancer, by causing a loss of valuable time may prove a menace to the patient's life. Radium has the great advantage of leaving no

scar, there is practically no danger of burning, and it is pleasant to the patient. Unfortunately, its action is slow, and usually the patient must be under observation and treatment for a long time.

Granted an accessible growth, actual cautery or excision and cautery would seldom fail if the surgeon did not have cosmetic results in mind. In practice it is not infrequently necessary to cauterize small recurrences at the site of the previous operation. These are usually small if the patient is warned to return for treatment at the first sign of a new-growth. Superficial growths of small extent need simply to be cauterized, and, for this purpose, the electric cautery or the Paquelin answers very well. Larger or adherent growths are better excised, cutting well into the sound tissue and burning the entire wound with the soldering iron. The wound is packed with boric-acid powder and bandaged. In cancers involving the canal to any extent this is more difficult, and involves in some cases an occlusion of the canal. In most cases grafting is not necessary, since the scar is apt to be surprisingly good cosmetically and the patients have arrived at an age when some scar is preferable to the inconvenience of a graft. The cauterized tissue, however, sloughs off easily and furnishes a good bed for graft in a couple of weeks.

Radical local excision without cautery is permissible in non-adherent growths so circumscribed that there is no question of the whole growth being removed. The element of safety in the cautery lies, not only in the killing of any seed-cells that may have remained in the wound, but also in the deep cooking given the tissue beyond the reach of the knife. This is seen especially in growths adherent to bone or cartilage. What statistical data I have been able to collect support the use of cautery in addition to excision.

*Prognosis.*—We have completed records of two cases with glandular involvement operated on. One of these should be classed as exploratory because the operation showed such extensive involvement of the middle ear and mastoid that further work was abandoned. The one cured had radical removal of glands,

and is still healed after seven months. Of the completed cases in the literature, 3 died and 2 were cured (time given in one case only, eleven months). It should be mentioned that of the 3 patients who died, only one had a radical removal of glands, whereas both those cured had the glands excised as well as the growth. Small as these figures are, they offer very good justification for operation in cases with glandular involvement.

Of the cases without glandular involvement, two-thirds were cured; in the literature, 50 per cent. Judging from the character of our cases not heard from or seen subsequent to operation, I should put the percentage of recovery considerably higher. Of those that were not cured, all were adherent to the cartilage. It should be emphasized here that percentages given are not to be regarded as absolute, since the number of completed cases is too small; they were computed merely to serve as indicators. Conditions unfavorable to cure are adherence, actively growing type, and wide spread of involved area. Mere duration is of itself of little importance, save that long duration before consultation usually means a very inactive type of growth.

To conclude: (1) Epitheliomas of the external ear are peculiarly resistant to treatment, and hence should be treated early and the patient kept under observation at least six months.

(2) The best method of treatment is radical local excision and actual cautery. Because of the infrequency of glandular involvement, dissection of glands should not be done routinely. Glandular involvement does not render the case inoperable if competent surgical service is at hand.

(3) Radium and the Roentgen-ray should be reserved for small, superficial, slow-growing epitheliomas. The actual cautery is as effective in such cases and saves much valuable time. Caustic pastes, very effective in skilled hands, are so closely associated with cancer quacks that it would seem desirable not to lead the people to have confidence in them.

(4) Chronic suppuration of the middle ear acquires an additional menace from its relation to cancer.

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## ANAPHYLAXIS AND ASTHMA \*

JUSTUS MATTHEWS

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Anaphylaxis is one of the most fruitful and interesting fields of research to which the attention of medical scientists has been directed during the past decad. In it has been found explanation, not only of certain phases of immunity and hypersusceptibility to infections, but also of various diseases and symptoms, such as asthma, hay-fever, serum disease, urticaria, etc., which are apparently of far different origin. We have thus been enabled to group and study logically by animal experimentation these conditions in ways that promise still greater revelations for the future.

Although observations of anaphylactic reactions had been made previously, no very extensive systematic experimentation was recorded until after the Theobald Smith phenomenon was reported in 1903. Immediately following this, researches by Rosenow and Anderson, Otto, and others began to yield results truly startling in their relation to many common clinical problems.

The serum disease was among the first of the phases of anaphylaxis to be carefully studied as to its etiology, symptomatology, and pathology. The blood or serum of many animals, when introduced parenterally into the blood or tissues of certain other animals, is more or less toxic. But men, rabbits, guinea-pigs, and other animals receive horse serum without reaction, except in the cases of individuals having the state of hypersusceptibility called allergy or anaphylaxis. The reception of the initial dose of serum by an animal not previously sensitized may or may not induce symptoms. The absorption of the second dose of serum from the same

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species will, under favorable circumstances, produce a changed or allergic reaction. It has been found subsequently that a great variety of protein substances will produce the anaphylactic reaction, but that symptoms of reaction are essentially the same in animals of the same species no matter what antigen be used. An animal sensitized to a certain protein may react to certain other proteins, but the maximum of reaction occurs only when the protein of both the sensitizing and toxic doses are taken from the same species of plant or animal. The condition of anaphylaxis may be either congenital or acquired. Inherited anaphylaxis is found in a portion of the offspring of sensitized females.

Acquired anaphylaxis may be either active or passive. Active anaphylaxis is produced by the parenteral absorption of a foreign protein, and requires an incubation period of six to twenty-one days. Passive anaphylaxis occurs only when artificially produced by the injection of the blood or serum of a sensitized animal into another animal of the same or another species. It requires an incubation period of only one day at most and may be immediate. After hypersusceptibility has been established it persists throughout life, but probably diminishes slowly and constantly after its maximum at about twenty-one days. A condition of anti-anaphylaxis usually follows recovery from an anaphylactic shock, but it is a transient phase and disappears after a length of time proportionate to the violence of the reaction.

Anaphylactic reaction to the toxic dose of antigen may be immediate or delayed. Immediate reaction or shock exhibits a variety of symptoms of which the most important is dyspnea. This may become extreme and end in death from asphyxia. It was at first assumed, from inconclusive experiments by Gay, Southard, and others, that the dyspnea was caused by the emphysematous condition of the lungs due to violent contraction of the diaphragm under control of the central nervous system upon the respiratory centers of which the antigen acted. The more recent experiments of Auer and Lewis have, however, demonstrated conclusively that both of these hypotheses were errors. Distention of the lungs persists after their removal from the thoracic

cavity, indicating that the emphysema is an effect and not the cause of the distention. Moreover, by various ingenious methods of recording at the same time the variation of intrathoracic pressure and the flow of air to and from the lungs during anaphylactic shock, they discovered that although the former were equal to or greater than normal, yet no air entered or left the lungs, which remained in a state of extreme distention. This was found to be due to tonic contraction of the muscular coat of the bronchioles which prevented the escape of air from the alveoli. Sections of the lungs of animals dead of anaphylactic shock are dry, showing that neither pulmonary edema nor hypersecretion of viscid mucus plays an important part in the occlusion of the alveoli or bronchioles.

The solution of the question as to whether the phenomenon of shock depended on the central or peripheral action of the antigen was equally conclusive. Section of both vagi had no effect on the character or severity of anaphylactic shock, whether the antigen was injected immediately after the section or after an interval of time sufficient to allow complete atrophy of the peripheral nerves. The use of curarin for the same purpose was also lacking in effect, although the superficial appearances varied somewhat on account of the necessary use of artificial respiration. Likewise, in a pithed animal the toxic dose was followed in from one to three minutes by gradual decrease of respiratory oscillations until the rhythmic blast could force no more air into the distended alveoli, from which tonic contraction of the bronchioles prevented its escape. Thus it appears that the reaction may and probably does normally occur without the assistance of the nervous system. The demonstration by Schultz that pieces of smooth muscle from a sensitized animal would contract far more upon contact with the specific antigen than would similar pieces taken from normal animals supports this view, by showing that the antigen may act directly upon the muscles of the bronchioles.

Under certain conditions animals may be sensitized by the taking of an antigen into the stomach, as guinea-pigs become sensitized to the horse by the eating of raw horseflesh, and will



give the characteristic anaphylactic reaction to the serum or other tissues of the species.

The many individuals who suffer violent gastro-intestinal and sometimes respiratory disturbances on taking certain articles of food are undoubtedly subject to the same reaction. This is caused by the absorption into the blood and lymph-channels of a protein which has not been sufficiently digested to lose its identity and which thus becomes an antigen capable of producing the same reaction as though introduced parenterally into the blood or tissues.

Guinea-pigs become sensitized to the horse by confinement in the same room, through the inhalation of emanations, and it seems probable that the individuals who are sensitive to the horse, cat, or other animal have received their sensitization in the same way. The majority of the deaths following the therapeutic injection of horse serum have occurred in persons subject to horse fever and asthma or in those sensitized by previous injections. The symptoms in these cases, while exactly typical of anaphylactic shock, are those of an extreme asthma resulting in asphyxia and death. Hay-fever, rose-cold, and similar affections occur in those individuals whose membranes are hypersensitive to specific varieties of pollen and their symptoms are analogous to and undoubtedly identical with the local reaction of experimental anaphylaxis. The asthma often associated with the local symptoms of hay-fever is induced by the entrance of the same antigen into the blood or tissues, usually through the mucous membranes of the upper respiratory tract, and is the typical respiratory disturbance of acute non-fatal anaphylactic shock. Clinically, asthma produced by these known foreign proteids differs in no respect from the more common form of the disease known as spasmodic or bronchial asthma, except that in the latter the identity of the foreign protein causing the reaction is unrecognized.

Susceptibility to anaphylaxis has been observed to vary greatly in individuals, families, and varieties of guinea-pigs. The so-called asthmatic tendency has in a similar way long been known to be marked in certain persons and families, and heredity has undoubt-

edly an important bearing on the etiology of the disease. It has been assumed that this predisposition was inherent in the nervous system, and this may be so in some cases, but there is no proof of this assumption, whereas it has frequently been observed that many of the individuals subject to heredity have very evident etiologic factors in nasal polyps, suppurating sinuses, etc., the removal of which has relieved the asthma. From this it would appear that the essential inheritance has been an anatomic or functional predisposition to affections of the upper respiratory tract, probably associated with a susceptibility to anaphylactic sensitization. This makes it especially important to favor in every possible way the development of the upper respiratory tracts in children who might be expected to inherit this tendency.

Osler states that diseases of the lungs are rarely if ever the cause of asthma, and the fact that the emphysema and bronchial lesions commonly associated with asthma of long standing are rarely if ever seen in early cases, favors the belief that these conditions are results and not causes of asthma. However, it is not improbable that severe chronic bronchitis, especially if associated with bronchiectasis, whether or not the result of asthma, may, in certain cases, furnish the site for the retention and reabsorption of mucous secretions. The cures obtained by treatment with the bronchoscope in a series of such cases after all other means had failed, as described by Horn, Freudenthal, and others, would agree with this hypothesis.

An interesting case illustrating some of these points was that of a young girl who suffered violent symptoms of anaphylaxis on contact with wheat flour. In early childhood she had fallen head foremost into a partly filled barrel of flour, by which she was nearly strangled. Quantities of flour were inhaled and she probably absorbed undigested proteins from it through the mucous membrane of some portion of her respiratory tract. Since that occurrence any dust of flour in the air has occasioned severe hay-fever and asthma, and the eating of incompletely cooked wheat flour has sometimes caused violent gastro-intestinal as well as respiratory disturbances. Urticaria has often followed these attacks. The

recurrence of the nasal reaction occasioned by the contact of flour has gradually resulted in chronic rhinitis and ethmoiditis, with polypoid degeneration of nasal mucous membrane of the region. During the past winter she has had asthma without the agency of flour and evidently caused by the pathologic condition of the nose, since it ceased promptly on the correction of the local lesions.

The development of chronic rhinitis and sinusitis by the recurrence of vasosecretory disturbances in cases of recurring hay-fever is a logical sequence and has been commented on by many writers. Asthma likewise is a frequent accompaniment of hay-fever and will usually be found to correspond in time and severity of occurrence with the pathologic changes in the nasal structures. At first it occurs only on exposure to contact with the specific external irritant which causes the hay-fever, but later develops a tendency to recur without this contact. Therefore, it is evident that there has developed another substance capable of acting as an antigen, and, since the pathologic conditions of the nose and nasal sinuses furnish a new factor in the retained and changed mucous secretions, it seems reasonable to look on this as the probable cause of symptoms.

Pus and mucus aspirated from the antra of asthmatic and non-asthmatic patients were used by Sanford (Mayo Clinic) as antigen in a series of experiments on guinea-pigs. The initial dose was received in each instance without symptoms, and the reaction to the toxic dose was uniformly the typical shock ending in death. This proves that mucus as well as pus is capable of acting as an antigen, and that the products of bacteria are not essential in producing either sensitization or shock. Further experiments are being carried out, the results of which would have a more important bearing on the subject of this paper and which I had hoped to report at this time. But failure to obtain a sufficient amount of proper material to give conclusive results makes it necessary to delay the report.

During the past four years there have been examined in the Mayo Clinic about 300 cases of asthma which I will not report in detail, as the series differs only in numbers from the report pre-

viously made. In over 90 per cent. of the cases the principal lesions which might be considered as etiologic were in the upper respiratory tract. Chronic suppuration or the retention of mucoid secretions in the nose or accessory sinuses occurred in the majority of these cases. Treatment was given with the object of securing free and continuous drainage of every portion of the tract and little attention was paid to possible reflex factors of etiology. In the majority of the cases the relief of the asthma corresponded almost exactly with the degree of success in obtaining the result sought, that is, the prevention of the retention and reabsorption of mucous secretions. The relief of asthma by any known treatment does not mean that the patient is permanently cured, since the susceptibility remains through life and symptoms will recur whenever there exist conditions favorable to the production and absorption of the specific antigen to which the individual is sensitive.

Various methods of desensitizing animals have been discovered, but no method yet reported gives a lasting immunity and all are attended by high mortality. Until a safe and efficient method of desensitization is possible the treatment of asthma must be directed, as in the past, to the relief of symptoms by whatever measures are indicated in each individual case.

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## POST-OPERATIVE HYSTERIC HICCUP \*

GORDON B. NEW

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The following is a case of post-operative hiccup which persisted for a period of five months and then was cured by a measure so simple that I feel warranted in making this report:

Miss G., aged twenty-one years. Family history negative. She gave a history of having had the following operations elsewhere: June, 1908, appendectomy; September, 1909, stones removed from left kidney; January, 1910, nephrectomy, left kidney. From January, 1910, to January, 1911, the sinus following the removal of the kidney was cureted several times; February, 1911, removal of capsule of left kidney. After each operation the patient had hiccup lasting from one to twelve hours. Following the last operation (in November, 1911), she had spells of hiccup lasting from a few hours to five days, coming on about once a month, until in April, 1912, the hiccup began and persisted continuously day and night for a period of five months. The patient was of medium height, thin, weighed 89 pounds, having lost some weight since the onset of the hiccup, and was rather nervous. The general examination revealed scars of the abdominal operations, some general tenderness over the abdomen, a discharging sinus in the left iliac fossa, and a moderately enlarged thyroid. The x-ray of the kidneys was negative. Cystoscopic examination showed a normal right kidney, but no secretion from the left ureter. The urinalysis, twenty-four-hour specimen, showed 900 c.c.; specific gravity, 1008; reaction neutral; a trace of albumin; a few blood-cells; a small amount of pus. An examination of the larynx was negative. The hiccup consisted of an inspiratory spasm of the diaphragm, glottis, and muscles of the neck and face, and made a noise like the "whoop" in whooping-cough, which could be heard a considerable distance. The rate of the hiccup varied from 20 to

\* Reprinted from the St. Paul Medical Journal, September, 1913, pp. 465, 466.

72 to the minute. Many measures to obtain relief had been tried elsewhere, but all of them failed. The patient was examined by C. H. Mayo (August 28, 1912), who believed that her nervous condition and not her physical condition was causing the hiccup. Intubation was advised and performed by the indirect method with the largest size of O'Dwyer tube. The hiccup stopped immediately, but started again in about three hours, when the tube was coughed up. Twelve hours later the tube was again inserted and remained in place eight hours before it was coughed up. The hiccup did not reappear and the patient went about like a different individual. A communication from her four months from the date of intubation stated that she had been quite free from hiccup with the exception of one slight attack, which lasted one and one-half hours. After that there was no further trouble.

Hiccup is not only a most distressing symptom, but at times is quite serious, and may result fatally, especially in elderly people. The attacks are intermittent; there is a sudden contraction of the diaphragm and glottis, the efferent impulses for which pass through the phrenic nerve to the diaphragm and the laryngeal branch of the vagus to the glottis. The characteristic sound is made by the sudden contraction of the glottis on the inrushing air caused by the sudden descent of the diaphragm. The efferent impression may be central or peripheral. Central irritation in tumor of the brain, apoplexy, or epilepsy may be found to be the cause; hysteria is also accountable for many cases, and these are usually the most obstinate to cure. Older writers report cases of several years' duration which were caused by hysteria, and in which occasional cessation of the spasm avoided a fatal termination. Affections of the abdominal viscera, *e. g.*, appendicitis, chronic interstitial nephritis, intestinal obstruction, etc., may be the cause reflexly, or some direct irritation of the diaphragm, as the drinking of hot fluids, carcinoma of the esophagus near the cardia, or diaphragmatic pleurisy, may bring on the spasm. Chronic alcoholism, lead-poisoning, typhoid fever, malaria, diabetes, and uremia are frequently associated with hiccup.

Bassler\* reports two cases of singultus gastritis nervosus in

\* Bassler: New York Med. Jour., 1910, vol. xcii, pp. 311-313.

which the prominent symptoms were hyperesthesia of the stomach and hiccuping. No definite symptoms of hysteria were present, and the patients had lost much weight. He differentiates this type of hiccuping from the true hysteric type by the persistent gastric symptoms and the marked deterioration in the general health.

In the case reported the hiccup at first undoubtedly was due to the abdominal irritation, but later developed into a nervous condition. In a search of the literature we failed to find a report of the use of intubation in the cure of hysteric hiccup.

# THE INTERCAROTID PARAGANGLION AND ITS TUMORS\*

SURGERY BY DONALD C. BALFOUR. ANATOMY, PHYSIOLOGY, AND PATHOLOGY BY FRANZ WILDNER

## SURGERY

Tumors of the intercarotid paraganglion have, as a rule, been found malignant when recognized as such, and recurrences following their removal are frequent. Whether this be due to the fact that the tumors are seldom operated on in an early stage or because of a high degree of primary malignancy is not clear. In the cases heretofore reported the tumors have varied considerably in size, and frequently have been designated as perithelioma in type. The diagnosis is rarely if ever made before operation, and usually not until pathologic examination reveals the histologic picture.

The removal of a tumor of this gland, because of its situation and malignancy, often entails somewhat drastic measures. Its position in the carotid notch in certain cases necessitates ligation of one or all the main arterial trunks. In the case reported herewith removal of 4 cm. of the internal jugular vein was necessary.

The patient operated on in the Mayo Clinic was a woman, thirty-four years of age, who came for examination because of the distress incident to a large degenerating adenoma of the thyroid. The history of the patient was not suggestive, except in regard to the gradual increasing pressure and severe pain radiating through the right shoulder and down the right arm. The physical examination revealed an enlargement of the thyroid 5 by 6½ inches, marked evidences of obstruction in the deviated trachea, and the

\* Presented before the Society of Clinical Surgery, Rochester, October 10-11, 1913. Reprinted from *Surg., Gyn. and Obst.*, February, 1914, pp. 203-213.



dysphonia. Laryngoscopic examination demonstrated a paralysis of the right vocal cord. Otherwise the physical findings were inconsequential.

On April 5, 1913, under light ether anesthesia, the right lobe of the thyroid which contained the degenerating adenoma was removed. After completing the removal of the gland and ligating the vessels, further investigation revealed a separate mass in the right submaxillary region, about the size of a lemon, having the appearance of a degenerating fetal adenoma. At first this was believed to be an aberrant thyroid, but on attempting its removal it was discovered to be of an entirely different character, suggesting the probability of some malignant condition. The tumor was firmly adherent to all the surrounding structures, and apparently had been crowded up into the submaxillary triangle by the enlarged thyroid. After freeing it in front and below it was found on deep dissection to be intimately connected with the deep vessels. The mass was dissected from the carotid vessels, but it had invaded the internal jugular vein, and it was necessary to remove about 4 inches of this structure. This invasion of the vein made certain the malignancy of the tumor, and although the growth was removed *en masse*, it seemed probable that more or less rapid recurrence would take place.\* The field of operation was swabbed with Harrington's solution, and a twenty-four-hour pack of the same used to inhibit implantation of malignant cells. The patient's convalescence in the hospital was uninterrupted; she left on the sixth day. During her stay in town she suddenly developed a hemiplegia, which persisted until she left for her home. A recent report indicates the persistence of the hemiplegia and a probable local recurrence which will result fatally.

The after-history of patients in whom tumor of the intercarotid paraganglion has been removed is not encouraging. A cure without permanent disability is rare. Keen, who first called the attention of the American profession to the condition, states that only 7 patients of the 27 cases collected by him (including one of

\* Further description of the tumor may be found in this article under pathology.

his own) recovered without complications. Ordinarily, if the patient does not succumb to recurrence, some disability which is usually due to brain-lesion occurs.

## ANATOMY, PHYSIOLOGY, AND PATHOLOGY

### ANATOMY

In 1743 Albrecht von Haller found a nodule about the size and shape of a kernel of wheat at the point of bifurcation of the common carotid artery. Anatomic dissection revealed that the little body was inserted in the fibers of the sympathetic nerve plexus, which forms a dense meshwork around the common carotid artery and its branches; it may be found either at the crotch of the artery or in its immediate neighborhood, closely adhering to the wall of the vessel. The common carotid artery or one of its branches gives off a small vessel supplying the arterial blood.

Haller based his conclusions on the findings obtained by gross examination, and regarded it as one of the numerous ganglia distributed into the course of the sympathetic nervous system. He named it intercarotid ganglion, thus classifying it as a nerve-structure.

In 1862 Luschka made several hundred examinations with the object of studying its anatomy. The carotid body was found in every case. This author was the first to make detailed microscopic examinations of the tiny organ.

According to his findings, the carotid body is a globular or oval-shaped structure, measuring from 5 to 7 mm. in length, 2.5 to 4 mm. in breadth, and 1.5 mm. in thickness. It is found either in the bifurcation of the common carotid artery or on the posterior wall of the internal carotid, so that it is not distinguishable anteriorly. For this reason it has been termed retrocarotid body by French writers.

Its color is a grayish red up to a shade of purple-red, depending on the amount of blood filling the capillaries. It is fairly dense, and occasionally it may be broken up into halves, with more or less of a connecting link between, rarely in four or five particles

which are scattered over quite an extended area and in the course of the internal carotid artery. In this respect it resembles the parathyroids, of which especially the upper one is sometimes divided in two or more units, with occasional cell-groups in the lateral lobes of the thyroid completely surrounded by thyroid acini. A homologous organ is present in all mammalian animals at the bifurcation of the carotid or in its vicinity.

On microscopic examination Luschka found cells with a large protoplasmic body grouped into clusters and strands of various size, a large number of thin capillaries surrounding the cell-clusters, and very numerous sympathetic nerve-fibers with scant ganglion-cells. The parenchymatous cells were the characterizing feature, and, assuming their epithelial origin, he presumed that the anlage of the carotid gland buds off from the epithelium of a branchial cleft. He regarded the enigmatic body as a gland closely attached to the cervical portion of the sympathetic nervous system, and applied to it the term "intercarotid gland." He placed it in series with the adrenals, the anterior or glandular lobe of the hypophysis, and the coccygeal gland.

The carotid gland, the anterior lobe of the hypophysis, and the coccygeal gland, though differing in minor details to the extent of establishing their individual independence, are similarly constructed; *i. e.*, large cells resembling epithelial cells arranged into lobules of various size and shape, in close anatomic relation with the sympathetic nervous system. The coccygeal gland found just in front of the apex of the coccygeal bone and associated with the median sacral artery is about 2 to 3 mm. in diameter, and bears closer resemblance to the carotid than to any of the other glands. It is a constant single organ. Not infrequently it is represented by five or six small nodules. It contains a great number of capillaries and many fibers from the ganglion impar of the sympathetic.

These organs belong to ductless glands, blood-vessel glands, or glands with internal secretion, following Claude Bernard, who distinguished the external secretion of bile—through an efferent duct—from the storage and mobilization of glycogen as internal secretion.

It is interesting to note that thirty years before the first cases were reported by Marchand and Paltauf, Luschka expressed the opinion that the vestige of the carotid gland may give rise to the growth of tumors.

Arnold took a view different from that of Luschka. He was impressed by the large number of capillaries which occasionally formed whorl-like structures comparable to glomeruli, and concluded that the organ was characterized by a network of capillaries, the walls of which were coated by large cells. To him it was a vascular structure which he named "intercarotid arterial glomeruli."

Waldeyer accepted Arnold's view in the main. He regarded the large epithelial-like cells as especially differentiated cells of the adventitia of the capillaries, and therefore as constituents of the vessel-wall. He made a distinction between the endothelium of capillaries and the large perithelial cells, and introduced the term "perithelial organ" for organs built on the plan of the carotid or coccygeal gland.

A new era has been opened by Schaper's article on the histology of the carotid gland. He showed that many microscopic findings described as the carotid gland were artefacts, due to autolysis of the very unstable protoplasm of the cells. He emphasized the examination of fresh tissue, and demonstrated that only chromic acid or its salts were able to fix the cell structure in a way reflecting the picture of fresh tissue. He pointed out that the epithelial-like cell groups, notwithstanding their close relation to the capillaries, are independent of them, the capillaries showing a continuous endothelial lining and the same structure as elsewhere in the body.

Stilling agrees with Schaper as to the independence of the cells from the capillaries and finds that some of the cells take a brown tinge after fixation with potassium dichromate; the self-same cells are found in small corpuscles attached to the abdominal part of the sympathetic, which he is inclined to class as accessory adrenals. In summarizing he thus emphasizes the structural analogy of the carotid gland with the adrenals; "I believe to be able to confirm that the carotid gland, whatever be its embryonic

origin, is neither a simple vascular network nor a rudimentary organ, but a 'blood-vessel gland' of a structure analogous to that of the adrenal."

In a very logical investigation Alfred Kohn showed why so many authors, though unraveling numerous elements of truth, failed to arrive at a satisfactory explanation. They had studied the fully developed organ and had allowed themselves to be carried away by some dominant features on which they laid undue stress. They had in turn regarded the minute structure as a ganglion, a gland, an epithelial organ, a vascular organ, a rudimentary organ. Kohn took the position that the nature of an organ is determined by the nature of its specific cells. His was a histogenetic viewpoint, and he attempted to trace the development and the textural structure from the earliest stage up to the developed organ. First of all he disproved the alleged epithelial character of the cells. Epithelial cells are found lining outer or inner surfaces of the body; they show a clean-cut borderline toward the underlying connective tissue and a polar orientation, the free surface being differentiated from the base. The carotid cells are found in the midst of connective tissue, and heaped up without any trace of orientation or polarity. He concludes that the utmost lack of regularity as to size and arrangement of the cells rules out their epithelial nature, and contends that they are a type of cell altogether different from epithelial, endothelial, or perithelial cells. Another peculiar feature of the cells is the lability of their protoplasm. Specimens removed later than forty-five minutes after death showed marked changes of the cells due to autolysis of the cell-substance. Experimentation with the various fixing fluids proved that only chrome salt solutions are apt to fix and preserve the protoplasm in its natural condition, at the same time staining it often a faint yellowish tint or any shade from a light yellow to dark brown. All other fixatives, such as formalin, absolute alcohol, or sublimate, dissolve certain substances of the cell-body, the nuclei only remaining intact in a protoplasmic network with irregular meshes. Kohn named the cells "chromaffin cells," on account of their chemical affinity to chrome salt solutions. These cells are

large and mostly polyhedric, though very polymorphous in appearance; the protoplasm is almost homogeneous or faintly granular. The nucleus is round or oval, and shows a dense chromatin network with one or more nuclei and a sharply outlined nuclear membrane. Mitoses are found, though rarely.

A very large number of non-medullated nerve-fibers enter into the formation of the carotid gland; typical ganglion-cells are found scattered or in small groups in the sympathetic nerve-fibers. Kohn then proved, by comparative studies, the close relation between the cells of the carotid gland—the chromaffin cell—and

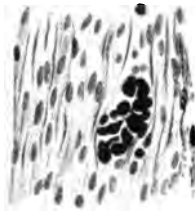


Fig. 265.

Fig. 265.—Sympathetic nerve from the vicinity of the carotid paraganglion. In the midst of it a group of chromaffin cells.

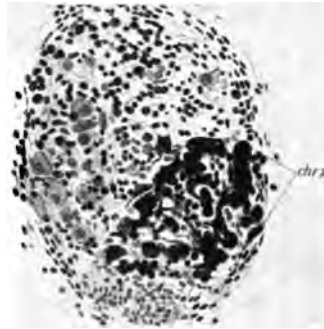


Fig. 266.

Fig. 266.—Sympathetic ganglion from the pelvic portion of the ganglion cord (fetus of seven months). One-half of the ganglion taken up by the chromaffin cells (*chrz*) (from A. Kohn).

the non-medullated nerve-fibers. He found groups of chromaffin cells embedded in the sympathetic nerve-fibers (Fig. 265), running to the carotid gland, much as ganglion-cells are interwoven into the tracks of nerves. In the supreme cervical ganglia of the sympathetic small groups of chromaffin cells are found. There is a continuous stretch of chromaffin cells extending from the carotid gland through sympathetic nerve-fibers to the supreme ganglion of the sympathetic. Here typical ganglion-cells, chromaffin cells, and nerve-fibers are found in closest union. The finding of the chromaffin cell—the characteristic element of the intercarotid gland—in sympathetic nerve-fibers and ganglia led to the as-

sumption of a closely allied kinship between the carotid gland and the sympathetic nervous system.

Small islets of chromaffin cells are found in the sympathetic nerves and ganglia from head to coccyx (Fig. 266). Large autonomous organs are built up in the retroperitoneal space in close neighborhood to the abdominal aorta. The most proximal part of the abdominal paraganglion dips down into portions of the Wolffian body, and the union of these two widely different organ-

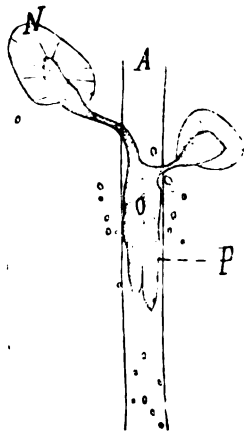


Fig. 267.

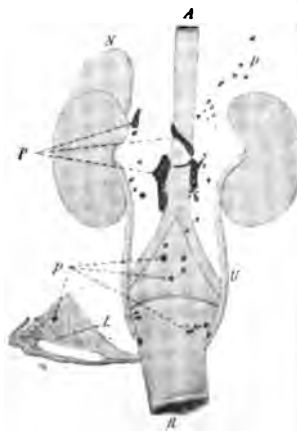


Fig. 268.

Fig. 267.—Paraganglion of a new-born rabbit. Diagrammatic drawing ( $\times 10$ ): *A*, Aorta; *N*, adrenal; *P*, aortic paraganglion forms the medulla of the adrenals with its cranial terminals (from A. Kohn).

Fig. 268.—Paraganglia of a girl (forty-five days old): *A*, Aorta; *N*, adrenal; *U*, ureter; *R*, rectum; *L*, broad ligament; *P*, *p*, major and minor paraganglia. On the left the adrenal has been removed in order to show the paraganglia on its posterior surface.

systems shapes the adrenal gland (Fig. 267). Its medullary part is a part of the sympathetic derived from the ectoderm, while the cortical part is part of the renal system derived from the mesoderm.

Another large paraganglion is the "accessory organ of the sympathetic" (Zuckerkandl), found at the site of bifurcation of the abdominal aorta, which is well developed in the new-born, being 10 to 15 mm. in length and 3 to 5 mm. in width. Small paraganglia are found in the space between the adrenals, kidneys,

and ureters, in the interiliac angle, in the mesorectum, and broad ligament (Fig. 268). All paraganglia outside the adrenal medulla undergo involution after birth.

The chromaffin cell, which is the structural unit of the carotid gland, the medulla of the adrenal, and the accessory adrenals of the sympathetic, is a derivative of embryonic cells of the sympathetic. The embryonic cells of the sympathetic-sympathoblasts differentiate into adult sympathetic ganglion-cells and nerve-fibers, but some of them form chromaffin cells, *a cell which retains to a certain extent the features of the embryonic ganglion-cells*. I believe that the undeniable epithelial appearance which so deeply impressed itself on many workers may be a heritage of the epithelial origin of the nervous system, which traces its derivation back to ectodermal epithelium. Thus the chromaffin cell is closely related to the ganglion-cell, but it does not form fibrils which are characteristic of the ganglion-cell. Like the ganglion-cell, it appears either singly or in smaller or larger groups embedded in the track of sympathetic nerves, or, like the more differentiated ganglion-cell, it may form individual organs. Kohn introduced the term paraganglion for organs made up of chromaffin cells to express their histogenesis from the embryonic ganglion-cell.

Another term, "parasympathetic organs," expresses their histogenetic and anatomic relationship. Chromaffin cells develop in all parts of the sympathetic nerve anlage, in the cervical as well as the abdominal and sacral part of the sympathetic system; yet in certain locations they form large aggregations and independent organs. The intercarotid paraganglion, the adrenal paraganglion,—the largest of the body,—and the abdominal paraganglion are all made up of chromaffin cells derived from the embryonic sympathetic cell. They all retain their initial kinship with the sympathetic system in the fully developed organism.

In the human new-born chromaffin tissue is very widely distributed, but an involution sets in in early life and no chromaffin cell is found in the adult sympathetic (rests of chromaffin cells remaining in the carotid gland and the adrenal). In mammals it is a permanent structure (Swale).



It has been shown in embryos of the cat, pig, and man that the cells of the intercarotid paraganglion develop from embryonic ganglion-cells of the sympathetic at the central side of the internal carotid artery (Fig. 269). While the majority of the embryonic sympathetic cells develop into typical sympathetic ganglion-cells and nerve-fibrils, a small number form sphere-shaped groups, the beginning of the alveolar structure of the Zellballen (Fig. 270). These sharply defined Zellballen are the unit of the adult intercarotid paraganglion; they take up at a later stage the chromaffin reaction. The fully developed organ then recedes from the wall of the internal carotid artery, and descends to a point at or near the bifurcation; on its way it has dragged sympathetic nerve-fibers with typical ganglion-cells along, leaving in its trail a few scattered chromaffin cells. Kohn's view of the nervous origin of the intercarotid paraganglion has been confirmed by subsequent investigations. It is interesting to consider that we have



Fig. 270.—Pig embryo, 87 mm. The cell alveoli (zb) have increased in size and multiplied. The organ shows the finished appearance (from A. Kohn).



Fig. 269.—Pig embryo, 45 mm. Section through nerve plexus (np) at ventral side of internal carotid (ci). Ganglion-cells in diffuse arrangement. Grouping of cells into acini (zb) the anlage of the carotid paraganglion (from A. Kohn).

returned to the position taken by von Haller in 1743. He based his sound and simple argumentation on the facts disclosed by gross dissection; slightly modified, his standpoint represents the best supported modern views.

In summarizing, one may say that the chromaffin cell—the structural unit of the intercarotid paraganglion—is found in the whole realm of the sympathetic nervous system, proving its histogenetic unity. Although the chromaffin cells are derived from the sympathetic nervous system, yet there is good evidence that they perform an internal secretion in adult life. The internal secretion of the adrenal has been established since the time of Addison in 1855. It is reasonable to use the term gland for secreting organs no matter what their morphologic origin is. Apparently the terms paraganglion and gland will be used promiscuously for the aforesaid organs, depending on the point from which they are viewed. There seems to be a close union between the nerve and vascular system in the paraganglia, the chromaffin cells throwing their secretion directly into the circulation under the stimulation of the sympathetic nervous system.

*Physiology.*—The intercarotid paraganglion shows, like all other paraganglia, an extremely rich vascularization. This fact in itself seems to indicate a very active metabolism. Only the largest paraganglion of the body, the medulla of the adrenal, has thus far received due attention. Adrenalin, when administered intravenously, will cause marked increase of arterial blood-pressure, due to its contracting effect on the unstriated muscle-fibers of the arterial wall combined with decrease in pulse-rate and increase of the force of the heart-beat. Glycosuria also results. Claude Bernard produced glycosuria by stimulation of a point at the floor of the fourth ventricle, and concluded that the stimuli traveled by way of the sympathetic system to the liver, causing a glycogenolysis. In recent studies on rabbits it has been shown that this experiment fails after removal of the adrenals or severance of the sympathetic or splanchnic nerve. In the light of this additional knowledge it seems that stimulation of certain points of the brain may be conveyed in the track of the sympathetic to the adre-

nal medulla, causing a secretion of adrenalin with its glycosuric effect. Adrenals removed from animals on which Bernard's experiments had been made showed a lesser pressor effect on the vascular system than the intact adrenal; and microscopic examination disclosed diminution or absence of the chromaffin reaction of the cells of the medulla. The various stages of physiologic activity of the secreting cells correspond to definite morphologic pictures, and the secretion appears in the shape of droplets which are evidently thrown into the thin-walled capillaries.

Josue found in rabbits which he had injected for some time intravenously with three drops of adrenalin 1:1000 arteriosclerosis of the aorta and larger arteries.

There are some observations that seem to lead to the assumption of an important rôle played by the intercarotid gland. The wealth of sympathetic nerves running into it, the chromaffin cells in immediate contact with capillaries, only a thin endothelium intervening, the instability of its protoplasm, and its rapid autolysis after death, seem to indicate the presence of a highly sensitive chemical substance.

The writer was able to find only a single instance of an experimental investigation into the function of the carotid paraganglion. Frugoni cites Vassale, who noted, after bilateral destruction of the organ, a considerable glycosuria of a passing nature or cachexia leading to death. Frugoni showed that intravenous injection of 5 c.cm. press-juice obtained from the carotid glands of suckling calves would kill a rabbit in one or a few minutes; there were convulsions, paralysis of respiration, and failure of heart action. The blood of the injected animal lost its clotting property, and the visceral organs were markedly hyperemic. The main action seems to be on the vascular system. Small doses of extract have a depressor effect on the vascular system; it is antagonistic to adrenalin.

### PATHOLOGY

Marchand published the first case of a tumor of the intercarotid paraganglion in 1891. Paltauf reported four cases in 1892.

The most striking characteristic of all these tumors was their location at the angle of bifurcation of the common carotid and their close adherence to the wall of the arterial vessels. In four out of these five reported cases the tumors could be removed only with resection of the common carotid artery and its branches, while in the fifth case the tumor was shelled out without damage to the vessels. The tumors showed also a great similarity in their microscopic structure. Marchand concluded that the tumor was of a peculiar structure, which could be derived only from a certain well-defined anlage. Paltauf regarded the four tumors he reported as peritheliomas of the carotid gland. The conclusions arrived at by these two authors are the more convincing as they were drawn independently. Since then about 35 cases of tumor of the intercarotid gland have been reported in the literature. With three exceptions they were all removed by operation. The three tumors found at postmortem are among the smallest in the series, being about the size of an almond or English walnut. The typical location of the tumors is the angle of the bifurcation of the common carotid, the growth, as a rule, adhering to the wall of the artery. Sometimes the common carotid artery is seen passing into the tumor (Scudder); in other cases the arteries lie in deep grooves in the tumor.

When the tumor is firmly adherent to the wall of the vessel, its removal is feasible only after resection of the common carotid artery and its branches. In some cases the internal jugular vein, the sympathetic, vagus, hypoglossal, and lingual nerve have been removed together with the carotid tumor. In a few cases the tumor, being loosely attached to the wall of the vessel, could be shelled out without damage to the arteries, or with ligation of the external carotid only.

The size of the tumor, which is well encapsulated, may be that of an almond, usually that of a hen's egg, and in some cases of a goose-egg. Some have the shape of a potato, and have been termed "potato tumors" of the neck.

The color depends on the color of the tissue proper and the amount of blood filling the capillaries. It may be a white, reddish

gray, brownish red, or even dark purple. The transparency and the glossy appearance of a freshly cut surface have been noted in several cases, occasionally reminding one of a parenchymatous goiter. The consistence depends on the relative amount of cells and fibrillary tissue; it may be firm, hard, rather elastic, or sometimes as soft as brain tissue. The capsule is fibrous, smooth, thin, and contains a large number of thin-walled veins. Fine strands of connective tissue run from the capsule toward the center, producing a lobulated appearance, and a sponge-like structure is produced by the presence of very numerous enlarged capillaries. The cut surface is characterized by its homogeneity and evenness of texture. In several cases that came to postmortem a search was made for the intercarotid paraganglion at the bifurcation of the vessel and in the surrounding tissue, but no traces of it could be found, while it was invariably present and of normal size on the other side. It was further observed that the tumor derived its arterial blood-supply from the common carotid or from one of its branches near the bifurcation in the same manner as does the intercarotid gland. The stroma of the tumors is usually more developed in the center than on the periphery.

On going over the tumors of the intercarotid gland one is impressed by the almost perfect identity of the salient features of all of them. There are certain differences in the various individual tumors, and there are variations in the pictures of sections taken from various places, but these differences appear secondary and are due to degenerative changes that have taken place.

Microscopically the tumors show an alveolar structure, with thin capillaries forming the stroma. The cells of the alveoli are grouped irregularly, and show a homogeneous protoplasm without partitions between the individual cells. In other cases the cells are rather well defined, polyhedral, or round. The nuclei are round or oval, sharply outlined, showing a number of chromatin nodules immediately below the vesicular membrane, and resembling plasma cells. Mönckeberg noted in two of his cases that the protoplasm of specimens fixed in Müller's or Zenker's fluid showed excellent preservation, while another tumor fixed in formalin showed the

same foam-like structure of its cells as is shown by the formalin-fixed cell of the normal organ. He laid stress on this reaction as being the chemical proof of the origin of the tumor from the carotid gland. A few of the cells of one of his tumors took up the yellowish tinge characteristic of the chromaffin cell.

The capillaries show a continuous endothelial lining, the cells being set directly on the endothelium. The width of some capillaries is remarkable, and accounts for the porous structure of some of the tumors. Hyaline degeneration is apt to set in in the walls of the capillaries, especially in the center of the growth.



Fig. 271.—Case No. 82518. Outer surface of tumor with resected internal jugular vein at upper pole plugged by tumor tissue.

Syncytial cell groups and giant-cells are occasionally observed. Karyokinetic figures are seen in the tumors, sometimes in large numbers.

Tumors of the intercarotid paraganglion are made up of chromaffin cells, the elements which form the normal structure. Whenever a tumor of a paraganglion—a paraganglioma—is suspected, it should be fixed in a solution containing chromic acid or its salts.

A mixture of 10 volumes of 3.5 per cent. solution of potassium dichromate and 1 volume of formalin gives an excellent fixative. After twenty-four hours' fixation the tissue should be mordanted in the dichromate solution for two days, then treated in the usual manner. The intercarotid gland may be divided into several portions, and chromaffin cells found in places distant from the bifurcation. We may then find chromaffin tumors at a distance from the bifurcation, for instance, at the jaw.

The tumors of the carotid paraganglion are rather benign, slow-growing neoplasms. They begin as hypertrophies of the normal

organ, and grows five, ten, even thirty-seven years without causing any discomfort. Though they adhere very closely to the arteries, only one case hitherto reported (Marchand's) showed penetration of the arterial wall, and two small nodules of tumor-tissue in the lumen, one exactly at the bifurcation and another a little higher up in the external carotid.

In the case herein reported the tumor was removed from the right side of the neck of a woman thirty-four years of age. After multiple adenomas of the thyroid had been removed a mass was found lying high up in the neck running up to the angle of the jaw,

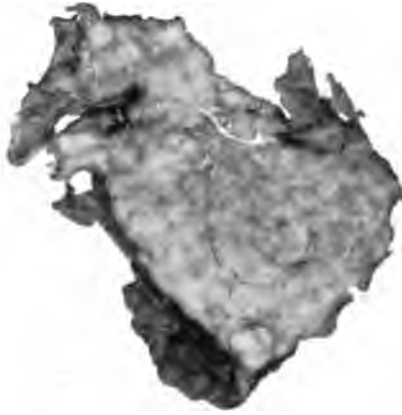


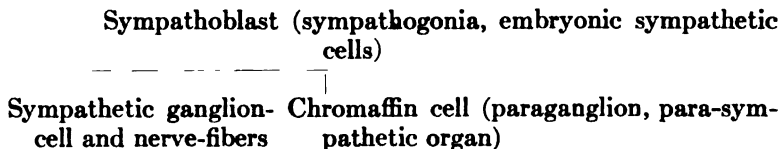
Fig. 272.—Case No. 82318. Cross-section of tumor shown in Fig. 271.

very densely adherent to all surrounding structures involving the internal jugular vein, a portion of which was removed with the tumor. The tumor measured 5 by 7 by 4 cm., was well encapsulated (Fig. 271), and could be shelled out without injury to the arteries. It was of a grayish-red color, very even on section, of a "live rubber" consistence and remarkable transparency (Fig. 272). The internal jugular vein was loosely plugged with tumor-tissue, 3 cm. in length. The microscopic structure is analogous to the previously reported cases (Figs. 273 and 274).

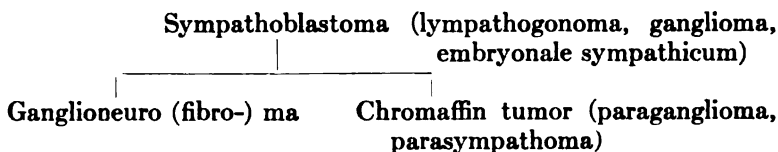
Metastases in lymph-nodes have been noted in a few cases.

Recurrences have been noted in about one-fourth the cases. Hyaline degeneration of the capillaries has been noted in a good many cases.

*Systemization.*—The study of the organogenesis of the intercarotid paraganglion has shown its origin from the primitive sympathetic anlage, and has attached this apparently isolated and vestigial corpuscle to the sympathetic nervous system. The embryonic sympathetic cell—sympathoblast or sympathogonia—develops into the sympathetic ganglion-cell and nerve-fiber, on the one hand, and the chromaffin cell, on the other.



It is interesting to examine the neoplasms of the sympathetic in the light of the facts put forth. Elements representing the various stages of embryonic development and differentiation may go into the making of sympathetic tumors.



Tumors consisting of these elements may occur at any point of the central nervous system, on the cerebrospinal nerves, on the sympathetic with its distribution, and in the visceral organs.

The sympathoblastoma may occur anywhere within the boundary of the sympathetic, preferably in the adrenal medulla of newborns or children. It is a malignant tumor with metastasis to the liver and other organs. Full-blown ganglion-cells and nerve-fibrils constitute the ganglio(neuro-)fibroma. They may arise from the ganglionated cord; they may be interposed between kidney and adrenal, or between spine and kidney. Wegelin found 14 out of 18



cases of the ganglionated cord on the left side. Herxheimer found among 28 tumors 17 arising from cord ganglia, 11 from the medulla of the adrenal or its vicinity.

A chromaffin tumor—a paraganglioma—may develop from any paraganglion of the body; so far only few tumors have been ascertained. These cases are tumors of the adrenal and intercarotid paraganglion and the coccygeal gland.

The adrenal medulla may develop all the possible tumors of the sympathetic tissue; the embryonic neuroblastoma, the ganglioneuroma, and the chrome-brown tumor or paraganglioma. The cortex of the adrenal produces the so-called adrenal hypernephroma as typical tumor.

Sacrococcygeal tumors should be carefully examined for the presence of chromaffin cells; they may be derived from the coccygeal gland. Tumors of the nervous system should be fixed in a formalin bichromate mixture in order to preserve the chromaffin cells.

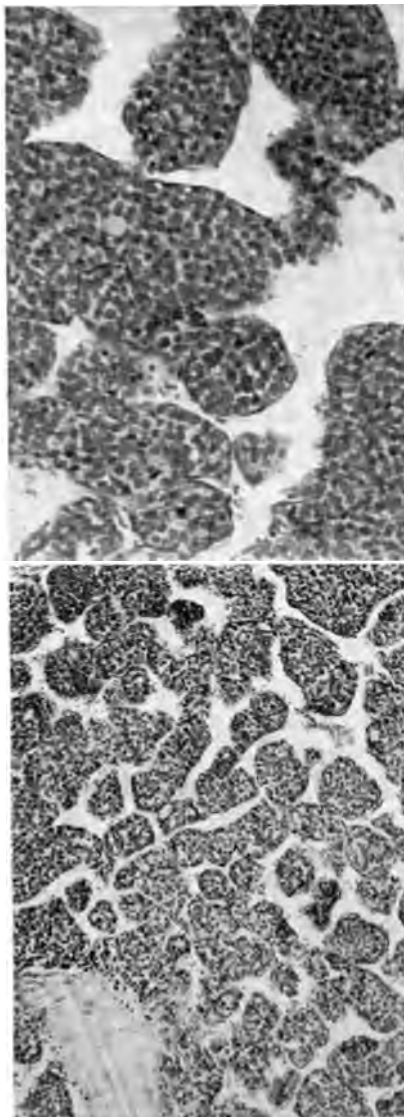


Fig. 274.—Case No. 82318. Same section, high power, capillaries with a continuous endothelial lining. Note the nuclei of endothelial cells.

Fig. 273.—Case No. 82318. Microscopic section, low power, showing the capillaries and alveolar cell-groups.

*Excessive and Defective Physiologic Activity Associated with Tumors of the Glands of Internal Secretion.*—What is the relation between the neoplastic cell and its normal mother-cell as to physiologic function? From microscopic examination, production of bile by the cells of a carcinoma of the liver and production of colloid in carcinoma of the thyroid have been known for a long time. The metastases of these tumors may occasionally secrete bile or colloid. Even under such conditions as exist in the bone-metastasis of a thyroid carcinoma, colloid in the acini has been seen. On the other hand, we have clinical evidence that the carcinoma of the thyroid may aggravate the symptoms of hyperthyroidism. A degenerating fetal or adult adenoma may produce toxic symptoms without exophthalmos.

Assuming a correlation between the changes in form and the changes in function, we may expect a hyperplasia of an organ to be combined with a hyperfunction, perhaps followed later on by hypofunction with the beginning of secondary tissue degeneration. Acromegaly is associated with an adenoma of the eosinophilic type of the anterior lobe of the hypophysis.

Tumors arising from the posterior lobe of the hypophysis may bring about the clinical symptoms of a high limit of sugar assimilation, adiposity, lowered blood-pressure, slowed pulse, subnormal temperature, asthenia, and drowsiness.

Neoplasms of pineal gland of young males may bring on rapid growth of stature, hirsuties, and a premature sexual development, with corresponding change of the frame of mind.

Of the tumors of the adrenal, we have to differentiate between those arising from the cortex and those from the medulla. The adrenal hypernephroma is apt to produce abnormal sex characteristics when present in females. The symptoms seem to be the more pronounced the younger the individual. Hirsuties, especially on upper lip, neck, chin, and chest, cessation of menses, atrophy of uterus and ovaries, obesity, and a change of voice have been observed; in men a gigantic increase in bodily strength has been observed.

Chromaffin neoplasms of the adrenal medulla with the symp-

toms of hyperfunction of the adrenalin-producing tissue were observed in a few instances. The clinical symptoms were those that can be experimentally produced by repeated adrenalin injections: glycosuria, hypertrophy of the heart, especially of the left ventricle, high blood-pressure, arteriosclerosis (found in a baby two years of age).

In view of these observations on the evidence of physiologic function in the cells of neoplasms of glands of internal secretion, one would expect to find evidence of the physiologic function in the presence of the enormous overgrowths of the intercarotid gland. In none of the reported cases of tumor of the intercarotid gland has a hyperfunction of chromaffin tissue been noted—perhaps one of the reasons may be that it has never been looked for.

Function, pathology, and clinical manifestations of the chromaffin system, the intercarotid gland in particular, are little known and the cases of tumor of the carotid gland have been usually diagnosed at the operating table, after having been designated as lymphoma or adenoma of the thyroid. The tumors of the intercarotid glands are by no means as rare as has been generally supposed. The Index Medicus lists three papers for the first six months of 1913.

It would seem rational that in cases of tumors of the carotid gland the whole chromaffin system be examined and evidence of its hyperfunction be carefully sought after. I would tentatively advance the hypothesis that the carotid gland tumor is but an anatomic expression of a functional disorder of the chromaffin system, affecting one or more units of the same. A bilateral overgrowth of the carotid gland has been observed by Enderlen.

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## CERVICAL RIB\*

### Report of 31 Cases

M. S. HENDERSON

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Cervical ribs are congenital bony deformities. They may be looked upon as a tendency to atavism. Every vertebra in certain lower forms of limbless vertebrates has ribs attached to it, but as we ascend the scale to the limbed vertebrates we find the ribs normally restricted to certain definite vertebræ. Occasionally in man lumbar ribs are found, but they are of anatomic rather than clinical significance, since they rarely if ever give rise to any discomfort.

Until within the last twenty years the cervical ribs that were recorded were considered anatomic anomalies only. Their presence had been noted by Galen in 1740 and perhaps the first authentic description was that of Hunwauld, published in 1742. A comprehensive description and classification was written by Gruber in 1849 in which he brought the reported cases up to 76. In 1894 Pilling collected 139 cases and reported them. Only 9 of these had been recognized during life. Since the Roentgen rays have come into use, however, the deformity has been recognized during life quite frequently.

The literature on the subject of cervical rib is abundant and that which was previously considered an anatomic curiosity has become established as a well-marked clinical entity. The anatomists reporting these early cases assumed that individuals thus affected had shown no symptoms during life. This was probably true in the majority of instances, but undoubtedly many had symp-

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toms which today would be diagnosed correctly, and the condition relieved.

In 1907 Keen published a paper on Cervical Rib and reported a case. It stands today as probably the best monograph on the subject in America.

While cervical ribs are congenital deformities, they rarely give symptoms until adolescence and well into adult life. There is no satisfactory explanation of why this is so, but probably they are slow of growth. In youth also we have greater elasticity of all tissues, and structures adapt themselves more readily to displacement. As an explanation for individuals complaining late in life Keen suggests that as we grow old the tone of the muscles is lost and the shoulders droop, thus increasing the angulation of the structure passing over the rib.

The deformity is usually bilateral. Of 31 cases observed in the Mayo Clinic, there were 24 bilateral. All the cases in this group in which there was undoubted elongation of the costal process on each side of the seventh cervical vertebra beyond the tip of the transverse process of the first dorsal vertebra were classified as bilateral. Nine of the 24 were well-developed bilateral cervical ribs, 10 were rudimentary bilateral cervical ribs, and 3 had a well-developed rib on the right side, with an accompanying rudimentary rib on the left. Two cases had a well-developed cervical rib on the left side with an accompanying rudimentary on the right. None of the males presented well-developed bilateral cervical ribs, while of the 10 presenting bilateral rudimentary ribs 6 were males. There were 5 patients with well-developed left cervical ribs, the right being absent, whereas there was only one developed on the right side alone. Of the 9 well-developed bilateral cervical ribs only 2 caused subjective symptoms and but one was operated on. In this case the left rib, which was the larger, was removed. The entire 9 objectively presented tumors of varying sizes in the supra-clavicular fossa. Of the 10 bilateral rudimentary ribs, 3 patients had subjective symptoms; in one of these patients the rib was removed. For some reason unexplained cervical ribs are more common in women—22 females and 9 males in this group. In

literature on the subject the percentage is usually rated as 70 per cent. of females and 30 per cent. of males.

It is believed by some observers that heredity has a bearing in the history of these cases, but this fact has not been noted in our observations. The occurrence of the deformity in connection with some other is often noted; in none of the 31 cases, however, was there any accompanying deformity. Marburg, Oppenheim, Borchardt, and Schönebeck reported cervical ribs in connection with syringomyelia, a condition for which it is frequently mistaken. Spiller and Gittings found the condition in a case of progressive muscular atrophy of the cervicobulbous type. Levi found it in a case of multiple sclerosis. These conditions may all have some bearing on the deformity, but probably are merely coincidents. It has been pointed out that scoliosis is quite commonly associated with cervical rib. Hibbing examined 400 cases of scoliosis by *x-ray* and found cervical rib in 2 per cent. The condition was not present in any of our cases.

As regards the relative frequency with which cervical ribs occur, no definite data can be obtained. Thirty-one have been recorded in the routine examination of approximately 80,000 patients in our clinic during the last five years. The chests of the patients are always examined, and any deformity in the supraclavicular fossa would be detected. Yet in the 31 cases there were 18 who gave no subjective symptoms. On physical examination 7 of these 18 patients displayed a fulness in the supraclavicular fossa, of which they may or may not have been cognizant. These patients were subjected to *x-ray*. Eleven of the 18 did not show a tumor, though after the *x-ray* had revealed the cervical rib a little fulness in some of the cases was detected in the supraclavicular fossa. This latter group of 11 cases had all been subjected to an *x-ray* examination of the chest for some other reason, *e. g.*, suspicion of tuberculosis, enlargement of the heart, substernal goiter, suspected aneurysm, etc. In none of them could the symptoms be attributed to the presence of the extra rib.

The lack of symptoms in the cases of this group is not to be accounted for by the age of the patient, since their ages ranged from

nine to fifty-one, with an average of thirty in the 18 cases. Undoubtedly, there were many patients who passed the routine examination in the clinic in whom cervical rib was present though not suspected. The chest not being x-rayed for any other reason, the condition was not discovered. At any rate, more than half the patients in our series gave no symptoms subjectively. The condition was discovered accidentally in the course of routine examinations.

Of the total number of patients (31), 6 gave symptoms subjectively and objectively, but were not operated on. In some instances operation was not advised owing to the absence of severe symptoms, and in others it was declined. The ages of the patients varied from nine to sixty. The patient sixty years of age (a woman) had had symptoms since she was fourteen. At the onset the pain in the left shoulder and neck was severe and continued for two years. The condition was not diagnosed and she gradually recovered, to be troubled only at intervals. There was present some atrophy of the left shoulder-girdle, the whole arm and thenar eminence, the arm being used with care. A tumor was noted about the time of the onset of symptoms.

Seven of the patients (5 females and 2 males) were operated on. Their ages varied from five to forty-nine years. The rib was excised in 6 of the cases; the other, a neurotic man aged thirty-eight, had alcohol injection and cautery to the neck. Both ribs were not removed in any of the cases.

On reviewing the literature, one is impressed by the wide range in the variety and degree of symptoms. A great many of the cases are diagnosed as brachial neuritis. In only two of our series had a correct diagnosis been made previously. A persistent neuritis over a term of years is usually the prominent symptom. A simple neuritis will have cleared up, as a rule, in a shorter time. Persistent neuritis in conjunction with a hard bony fixed tumor in the supraclavicular fossa on the affected side is almost positive evidence of the existence of a cervical rib, but the diagnosis can only be clinched by the x-ray.

In an endeavor to account for brachial neuritis from an ana-



tomic point of view, Jones intimates that persistent brachial neuritis may be caused by conditions other than cervical ribs, arguing his point from an embryologic standpoint. In the lower forms of vertebrates, the reptiles, a rib is attached to each vertebra. As we ascend the scale to the lizards, a neck, waist, and limbs have developed. With the development of the limbs has occurred a sacrifice of ribs opposite those segments from which the limb arose. In the cervical region in man there might arise a certain lack of harmony in the point of exit of the nerve-roots and the first rib. An individual might have the normal number of ribs but the nerve roots make their point of exit a little low and the first dorsal rib rise a little high. The result would be pressure on the nerves and a brachial neuritis. Various degrees of this condition might be present. In certain cases the cervical ribs do not give symptoms, and here again the nerve-roots may make their exit high and so escape pressure. If their exit be low or normal, pain will ensue.

Before considering the symptomatology of these cases a brief résumé of the anatomy is essential. Cervical ribs usually arise from the seventh cervical vertebra, which was the origin in all our cases. They are usually bilateral. Occasionally they arise from the sixth cervical vertebra also. There is a marked variation in size, and it is impossible always to judge from the x-ray as to their length. The vertebrocostal articulation also varies. It either articulates directly with the vertebral body or with the disc. If the sternal end is free, it may be movable. We know that embryologically each cervical vertebra has a costal process which, with the transverse process, forms the costotransverse foramen. The cervical rib arises as a result of the abnormally great development of this costal process, which process is traceable on all the vertebræ and in the thoracic vertebræ furnishes the normal ribs (Fig. 275). In the sacral segment it is so altered as to be scarcely recognizable.

Gruber's classification of these cases is the one generally adopted on account of its simplicity. He divides them into four groups as follows: (1) A slight increase in the costal process, not reaching beyond the transverse process. (2) When the rib protrudes be-

yond the transverse process to a certain degree and either terminates in a free end or is attached in some way to the first rib. (3) Those ribs which extend well beyond the transverse process and a considerable distance toward the first rib, even reaching the cartilage of the normal first rib. They possess a good body and are often united by a ligament to the first costal cartilage. (4) The rib which is completely developed articulating with the first costal cartilage and with the sternum. The cases coming under Group I (Gruber's classification) are not classified as cervical ribs.

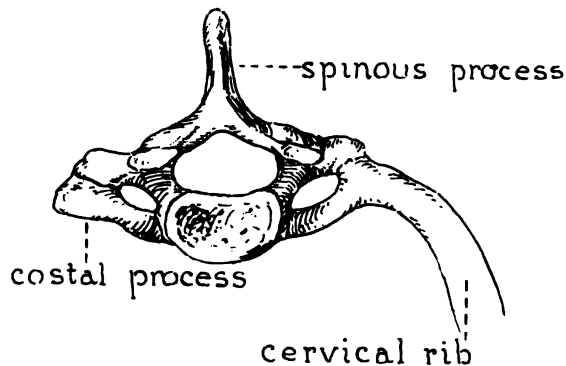


Fig. 274.—Showing abnormal development of the costal process into the cervical rib (from Morris' Anatomy).

Cervical ribs infringe on the territory of very important structures: the brachial plexus, the subclavian artery and vein, and the pleura. The pleural dome rises up into the neck, lies close to and is practically attached to the periosteum of this rib. It may be opened during operation, producing some degree of pneumothorax. This occurred in one of the cases in this report—the youngest, a child of five years—with no untoward result. The relation of the artery largely depends on the size of the rib. If the rib is short, the artery runs in front of it; if of fair size, it courses over it, but never has been noted to run underneath the rib. The scalenus anticus muscle is in front of the artery, thus placing the artery in a cramped position in an angle between the rib and the insertion of

this muscle, which fact has been ascribed as causing the arterial symptoms of gangrene of the finger-tips in the extreme cases before the true condition was diagnosed. This condition may indicate amputation, as recorded by Krabbe. Wingate Todd takes exception to the theory of gangrene due to mechanical obstruction to the blood-supply. He has carefully considered the anatomy of the subclavian artery and concludes that the constriction of the vessel at this situation is normal, as it is the top of the normal curve of the vessel. He states that this narrowing of the lumen of a vein to carry fluid at the top of a curve is a law of hydrodynamics. (Engineers copy this in their constructive work of this nature.) He believes that the clinical and anatomic evidence is sufficient to show that pressure on the sympathetic so disturbs the nerve supply to the vessels themselves as to decrease the blood-supply and cause gangrene. If the constriction be normal at this point, it would explain the increased caliber distal to this area, as has been noted by Murphy, Keen, and Ehrich. We do know that pressure on the vein is rarely evidenced, since edema does not often occur. The vein passes in front of the scalenus anticus, and so escapes the dangerous position accorded to the artery. Gangrene and nerve manifestations are said to be more common than edema. In our series was one case of edema, but none of gangrene.

The brachial plexus is usually involved to some extent as it passes down over the rib. Naturally it is the inner cord which is implicated, and this is spoken of as "the nerve of attack in cases of cervical rib." The region supplied by the nerve of Wrisberg and the ulnar are commonly affected. According to Howell, the route of the first dorsal nerve passes almost directly upward on the neck of the first dorsal rib, easily coming in contact with the cervical rib as it curves downward and forward. The variety of pains occurring in the neck, shoulder, and arm in different cases can all be explained by this irritation of the brachial plexus. The phrenic nerve, because of its course in the scalenus anticus muscle, is in close association with the cervical rib. Hunt reports a case of spasm of the diaphragm which was relieved by the removal of a cervical rib.

The symptoms subjectively fall under two heads: (1) nervous; (2) vascular. Wide variations are encountered in different cases. Under the nervous phenomena may be grouped neuralgic pains moving down the arm on the side on which is the large rib, as a rule. Numbness, tingling, and formication may be encountered and there is no constancy of the nerve involved, though it is usually the ulnar or inner cord of the plexus. There may be atrophy of certain muscles—the intrinsic of the hands and of the thenar and hypothenar eminences in particular. There is frequently atrophy of the whole arm, but this may be due to disuse, as these patients generally restrict the use of the affected member. Loss of power in the hand-grip may be noted. Marked cases may show distinct analgesia. Ataxia has been described by some observers, but was not present in our series. Hirsch's case showed sweating on one side of the arm and dryness of the skin on the other. Certain motions of the arm may cause marked neuralgic pains down the arm. These subside on rest, only to be brought about again by use. Some patients say they are relieved by raising the arms above the head and one of our patients slept in this position. Hoarseness is an occasional symptom. A girl of ten in our series had this symptom, but she also had an enlargement of the left auricle. Laryngoscopic examination showed a complete paralysis of the left cord, and the hoarseness was probably due to the enlargement of the auricle pressing on the recurrent laryngeal nerve as it passed up over the arch of the aorta. The pain may be all confined to the neck or pass up to the jaw and side of the face. One patient, a woman of forty-nine, had peculiar spasms of the larynx, which stopped her in the midst of a sentence, and also a sensation as though "her heart was coming up into her mouth." This occurred when she was under no emotional strain whatsoever. She had a steady pressure-pain at the left side of the sternum, passing up to the left side of her neck, even to her jaw. She described a feeling of pressure over the left side of the clavicle and occasional pains shooting down the left arm. There was some fulness of the left supraclavicular fossa, and she complained of tenderness along the left side of the neck to the left second rib. There was also an

element of neurosis to be considered. Pain was described which was irrelevant to the cervical rib. An aneurysm of the aorta had been previously diagnosed by a competent surgeon and she had been warned of its great danger. X-ray examination disclosed a left cervical rib. The rib was removed and the pain disappeared, but was replaced by a burning sensation which continued for six months. The pressure-pains and reflex laryngeal spasm ceased.

This case emphasizes a type of neurotic women who seem especially prone to have symptoms from cervical ribs, which is probably due to the fact that they have a hypersensitive nervous system which readily responds to the irritation of the cervical rib. Individuals with cervical ribs but with more stable nervous symptoms probably go through life oblivious of their presence. Four of the 7 patients operated on were of this neurotic type.

The vascular symptoms are less prominent than the nervous, but are equally as variable in intensity. There may be only slight coldness or there may be gangrene. Thrombosis has been reported extending up the arm and necessitating amputation. Pallor or erythematous patches may be present. Cyanosis may occur. Edema is rare, and in one of our cases was present not as a typical edema, but rather a suspicion of swelling in the hand of a woman of thirty-eight. A difference in the radial pulses is often referred to, but was not present in our cases. We also took readings of the systolic blood-pressure in each arm where there was any doubt, but these were the same. As regards the presence or absence of tumor or fulness in the supraclavicular fossa—in heavily muscled men there is not much to be made out. Thin people, and especially women, are more easily palpated, and here often the prominence is detected. The tumor is usually fixed, hard, and not tender. Often a distinct bruit may be heard over it, and aneurysm is suggested. X-ray is the only means of definitely clearing up the diagnosis.

*Technic.*—There are practically two methods of attack—the posterior and the anterior. The posterior incision is preferably a “hockey stick” over the anterior border of the trapezius. Dissection is made and continued down between the posterior border of the scalenus medius and the levator anguli scapulæ. In this

zone the nerve to the serratus as it passes through the scalenus medius is in danger. The advantage of this incision is that the brachial plexus comes down between the scalenus anticus and medius and is out of danger. The anterior incision is made through the posterior triangle of the neck and was the one used in all our cases. An incision is made about three or four inches in length an inch above and parallel to the clavicle, posterior to the sternomastoid. Dissection is then made down on to the rib, tying as many vessels as is necessary. By adhering closely to the cervical rib injury to structures is avoided. If the rib be large, the subclavian artery is on top of it; if small, the artery is in front of it. The vein is rarely seen. If the rib be large, it should be taken out in pieces, but if practicable, it should be removed whole.

#### CONCLUSIONS

1. Cervical ribs are congenital deformities, rarely causing symptoms until adolescence or later.
2. The deformity is usually bilateral (24 out of 31 cases) and is more common in women than in men (22 females and 9 males).
3. The size of the cervical rib is not the index to the symptoms.
4. It is estimated that only 10 per cent. of cervical ribs cause symptoms. Out of the 31 cases in this report, 18 gave no subjective symptoms.
5. Brachial neuritis may be caused by cervical ribs. This neuritis may be caused by a lack of harmony (embryologically) between the first dorsal rib and the site of exit of the roots of the nerves. The roots of the nerves may have their exit low and be subjected to pressure by a normal first dorsal rib or they may have a normal position and the first rib be high. We have had one case of brachial neuritis associated with tuberculous glands of the neck when during the course of the removal of the glands the first rib was seen to be high and to impinge on the nerves. It was removed with complete relief from symptoms.
6. The theory of the difference in the site of exit of the nerve-roots may explain the lack of symptoms in certain patients having well-developed cervical ribs, whereas other patients with smaller cervical ribs give pronounced symptoms.

## CASE REPORTS

*Group 1.—Cases Presenting no Subjective Symptoms*

CASE 1.—A45570. X-ray 10217. J. L., female, aged twenty-seven, married. Examination November 7, 1910. Operated



Fig. 276.—Case No. A45570. X-ray 10217. Mrs. J. L., aged twenty-seven. Physical examination showed fulness and tumor in left supraclavicular fossa. X-ray showed well-marked left seventh cervical rib rudimentary on the left; no definite symptoms. Operated on for double tuberculous salpingitis.

on for double tuberculous salpingitis November 15, 1910. X-ray taken to determine nature of tumor of left supraclavicular fossa showed well-developed seventh cervical rib on left; rudimen-

tary on the right. No symptoms traceable to the cervical ribs (Fig. 276).



Fig. 277.—Case No. A57933. X-ray 13135. Mrs. W. C., aged twenty-three. Came for examination because of pelvic trouble, for which an operation was performed. Fixed mass felt in right supraclavicular fossa. X-ray disclosed well-marked double seventh cervical rib, larger on the right side. No definite symptoms.

CASE 2.—A57933. X-ray 13135. W. C., female, aged twenty-three, married. Examination August 24, 1911. Dysmenorrhea. Operated on September 4, 1911, for retroverted uterus. X-ray



taken to determine nature of tumor in the right supraclavicular fossa disclosed well-developed cervical rib on right side and rudimentary rib on left, both seventh cervical. No symptoms (Fig. 277).

CASE 3.—A66420. X-ray 15139. G. T., female, aged twenty-eight, single. Nurse. Examination April 9, 1912. Chronic mastitis of the right breast. Tumors in both supraclavicular fossæ. X-ray disclosed double well-developed seventh cervical ribs. No symptoms attributable to ribs (Fig. 278).

CASE 4.—A62125. X-ray 14120. H. C., male, aged nine. Examination December 11, 1911. Condition diagnosed tuberculous meningitis. X-ray of chest for possible involvement of lungs showed double rudimentary cervical (seventh) ribs. Symptoms difficult to elicit, but no connection demonstrable.

CASE 5.—A58841. X-ray 13316. G. N., female, aged fourteen. Examination September 13, 1911. Chronic osteomyelitis right femur and subacute periostitis left humerus. X-ray taken for possible involvement of lungs showed rudimentary left seventh cervical rib. No symptoms arising from ribs.

CASE 6.—A62307. X-ray 14138. J. M. J., male, aged thirty. Examination December 15, 1911. Colloid goiter. X-ray taken for possible substernal goiter showed bilateral rudimentary seventh cervical ribs. No symptoms connected with the cervical ribs.

CASE 7.—A46957. X-ray 10536. J. T., female, aged forty-two, married. Examination December 13, 1910. Goiter. X-ray showed well-developed bilateral seventh cervical ribs. No symptoms from the cervical ribs.

CASE 8.—A68743. X-ray 15790. I. P., female, aged twenty-seven, single. Examination June 5, 1912. Abdominal symptoms attributed to adherent retroversion of the uterus and chronic appendicitis. X-ray taken to determine nature of bony prominence in the right supraclavicular fossa disclosed well-developed bilateral seventh cervical ribs. No symptoms caused by the ribs.

CASE 9.—A45473. X-ray 10197. E. R. H., female, aged fifty, married. Examination November 3, 1910. Headaches. Diagnosis: migraine. X-ray taken to determine nature of tumor in right supraclavicular fossa. There were some fulness, soft ex-

pansive pulsation, booming sounds, and questionable tracheal tug-



Fig. 278.—Case No. A66420. X-ray 15139. Miss G. T., aged twenty-eight. Well-marked double cervical ribs. No definite symptoms, though both ribs were palpable. The right rib clearly shows articulation with normal first rib. Note exostosis on first rib for articulation. Examined for chronic mastitis and operated on for this condition

ging. The picture disclosed well-developed seventh cervical ribs. No definite symptom traceable to these. A letter dated December

11, 1912, states that the ribs are "causing some uneasiness." Nothing further has been heard from the patient.

CASE 10.—A47490. *X-ray* 10647. W. J. S., female, aged thirty, married. Examination December 31, 1910. Indefinite neurotic symptoms. Had movable right kidney, of which she complained. *X-ray* taken to show condition of lung disclosed well-developed bilateral seventh cervical ribs. There was a little fulness in both supraclavicular fossæ. No symptoms attributable to the ribs.

CASE 11.—A30715. *X-ray* 5610. W. E. P., female, aged twenty-six, married. Examination November 1, 1909. Tumor of the sternum, which proved at operation to be chondrosarcoma. *X-ray* showed bilateral rudimentary seventh cervical ribs. No symptoms.

CASE 12.—A60436. *X-ray* 13649. B. H., aged twenty-three, single. Examination November 23, 1911. Chronic cough and hemorrhoids. *X-ray* of chest for possible tuberculosis disclosed well-developed left seventh cervical rib, none on the right. No symptoms.

CASE 13.—A69251. *X-ray* 15928. G. A. J., aged forty, married. Examination June 17, 1912. Diagnosis of urticaria (angioneurotic edema) and chronic constipation. *X-ray* of chest showed well-developed seventh cervical rib on the left. None on the right. No symptoms.

CASE 14.—A79871. *X-ray* 19293. J. B. R., male, aged forty-two. Examination February 11, 1913. One year previously, at his home, had had tumor of right cord removed which was pronounced malignant. At the time of examination in our clinic retroperitoneal involvement was evident. *X-ray* of chest showed well-developed left seventh cervical rib. None on right. No symptoms.

CASE 15.—A63471. *X-ray* 14430. W. L., male, aged twenty-nine. Examination January 26, 1912. Miner, and sustained injury May 15, 1911, by the caving in of a roof; was unconscious for fifteen minutes. Following this had numbness and loss of power in hands and arms. Much pain in back of neck. Had steadily improved up to date, though still some mild sensory disturbances in both hands and a little loss of power. No pain. *X-ray* showed bilateral rudimentary seventh cervical ribs. No lesion demonstrable in the vertebral column. The condition

was thought to be due to a lesion of the spinal cord and operation was not advised for removal of the cervical ribs.



Fig. 279.—Case No. A59085. X-ray 13437. M. D., female, aged ten. Came for consultation because of hoarseness for three months. X-ray of heart showed enlargement of left auricle; well-marked double seventh cervical rib. No definite symptoms from these. Died within a year of the cardiac trouble.

CASE 16.—A59085. X-ray 13437. M. D., female, aged ten. Examination September 25, 1911. Goiter and cardiac symp-

toms. X-ray taken to determine size of heart disclosed well-developed bilateral seventh cervical ribs presenting no symptoms. Paralysis of the left vocal cord was accounted for by the enlargement of the left auricle. A year later the child died of the cardiac condition (Fig. 279).

CASE 17.—A80479. X-ray 19598. C. T., female, aged twenty-five, married. Examination February 24, 1913. Operated on March 13th for dysmenorrhea. Patient also neurotic. Complained of peculiar bulging in supraclavicular fossa when coughing. No pains, numbness, or tingling in arms. X-ray showed bilateral seventh cervical ribs.

CASE 18.—A82512. X-ray 20504. J. P., male, aged forty-five. Came for consultation on account of sinus in neck following abscess caused by lodging of a seed in his throat. X-ray taken for this condition possibly due to diseased hyoid bone disclosed bilateral rudimentary seventh cervical ribs. No symptoms attributable to the ribs.

## GROUP II

### *Cases of Cervical Ribs Giving Subjective Symptoms but not Operated On*

CASE 19.—A56581. X-ray 12742. E. E., female, aged seventeen, single. Examination July 27, 1911. For four years had had shooting pains in right arm. Right thumb became cold and numb several times a day. Entire right hand loses feeling at the same time. Exacerbation of symptoms at time of examination. For four months had had frequent shooting pains in right leg as high as knee. Neurotic element present. Muscles of the right arm were weak, and arm was smaller than left. Sensations were not disturbed. X-ray shows bilateral rudimentary seventh cervical ribs. Operation was not advised on account of neurotic element.

CASE 20.—A38537. X-ray 8855. R. F. S., female, aged thirty-two, married. Examination June 7, 1910. Pelvic trouble. Hard bony masses were felt in both supraclavicular fossæ. X-ray showed bilateral seventh cervical ribs well developed. Indefinite mild pains down the arms were complained of, but not considered serious by the patient. Operation was not advised (Fig. 280).

CASE 21.—A57685. X-ray 13046. G. L. K., female, aged forty-five, married. Examination August 14, 1911. Indigestion.

Complained of a little numbness in right little and ring-finger. Also in right little toe and fourth toe. X-ray taken to prove the nature of tumor in right supraclavicular fossa disclosed large



Fig. 280.—Case No. A38537. X-ray 8855. Mrs. R. F., aged thirty-two. Came for examination complaining of pelvic trouble. Examination disclosed bony prominence in both supraclavicular fossae. Neuralgic pains of an indefinite nature down the arms. X-ray showed well-marked double seventh cervical ribs. Operation not advised.

right seventh cervical rib and rudimentary left. Operation was not advised (Fig. 281).

CASE 22.—A72278. X-ray 16753. H. C., male, aged forty-three. Examined August 19, 1912. Symptoms for eighteen months. Boring pain flexor surface of left arm. For the past

month occasionally the same pain in the right arm, worse on exertion, particularly in pitching hay. Lately increasing loss of



Fig. 281.—Case No. A57685. X-ray 13046. Mrs. G. L. K., aged forty-five. Came for examination complaining of indigestion. Probable cholecystitis. Adenomas of thyroid. Slight numbness in the right little and ring finger, also in right little toe and fourth toe. X-ray disclosed well-marked right seventh cervical rib. Rudimentary on the left. Rib barely palpable. Operation not advised.

power left arm and hand, with intense pain on use. Naturally left handed, but there was one-half inch atrophy at the biceps. Reflex

of the left biceps decreased. No numbness. X-ray showed bilateral rudimentary seventh cervical ribs. Operation was advised, but the patient was lost sight of. This patient was sent in by his physician with a diagnosis of tumor of the spinal cord.

CASE 23.—A36137. X-ray 8320. G. W. A., female, aged sixty, married. Examination April 5, 1910. History back to when fourteen years of age, when the patient had severe pain for several years in her left arm. Always some pain in left shoulder and along the neck. Some atrophy of left shoulder. About time of onset tumor was noted above left clavicle. Always some discomfort with exacerbations. Some atrophy of supraspinatus muscle and thenar eminence on left side. Handled left arm carefully. X-ray showed well-developed left seventh cervical rib. None on the right side. Operation was not elected on account of the age and disinclination of the patient, who did not consider the symptoms serious enough for operation.

CASE 24.—A80360. X-ray 10529. V. H., female, aged twenty-four, single. Examination February 20, 1913. Complained of pains in hands and arms after using them. Hard work at stenography for four years. Was well until the summer of 1912, when she began having shooting pains in hands and wrists spreading up the arms. Forced to discontinue work for a week. Improved with rest; on resuming work the pains recurred and she had not worked since December. Physical examination negative. X-ray showed bilateral rudimentary seventh cervical ribs. Operation advised but deferred up to date.

### GROUP III

#### *Cases Operated On—1 Palliative, 6 Radical*

CASE 25.—A12860. X-ray 2765. J. L. N., female, aged forty, married. Examination July 28, 1908. Patient complained of a fixed bony mass in the right supraclavicular fossa. She had known of this mass since childhood, but of late years it had grown steadily; more rapidly within the last six months. Since the patient had been operated on eight years previously elsewhere, having ovaries, tubes, and uterus removed supposedly for cancer, she was alarmed. On operation August 3, 1908, a good-sized right-sided seventh cervical rib was removed. The patient has not been heard from since being discharged.



CASE 26.—A31940. X-ray 5800. W. P., male, aged five. Brought by parents on account of hard, elongated tumor in right supraclavicular fossa. Examination December 8, 1909. The child had no subjective symptoms, but the parents wished the tumor removed. Measurement of the arms the same. December 18th a fully developed right cervical rib which articulated behind with the seventh cervical vertebra and in front with the first rib was removed. It was taken out in pieces. The pleura was opened with no bad effect. X-ray did not reveal cervical rib on the left side. Recovery was uneventful. The patient has not been heard from since he was discharged.

CASE 27.—A35026. X-ray 8086. W. R. J., female, aged twenty-nine, married. Had been examined in the Mayo Clinic four years previously. Cervical rib, left side, was diagnosed and operation advised, but was deferred. Symptoms now the same, though aggravated. Lump in left side of neck growing larger; pain up left side of neck and head to eye. Pain down to left shoulder. Arm swells at times. Collars seem too tight. Fulness in both supraclavicular fossæ, especially on the left. Here a thrill and bruit were discovered. X-ray disclosed double well-developed cervical ribs. March 10, 1910, the left cervical rib was removed. The right was not removed, as it was giving no symptoms. The patient's recovery was uneventful. She has not been heard from since one month after operation (Fig. 282).

CASE 28.—A41366. X-ray 19769. L. M., female, aged thirty, married. First came for examination August 6, 1910. Her symptoms indicated neurosis, and a diagnosis of such was made. She returned March 4, 1913. During the interval her symptoms had become aggravated, particularly pain in the right arm moving up to the chest. Most of the pain, which was dull and persistent, extended up the dorsal surface of the right forearm and the inner surface of the arm. X-ray disclosed bilateral rudimentary seventh cervical ribs. March 10, 1913, a rib  $\frac{3}{4}$  inch long projecting into the muscles, and over which the middle trunk of the brachial plexus was resting, was removed. The patient's recovery was uneventful.

CASE 29.—A44245. X-ray 9949. H. R. F., female, aged forty-nine, married. Came for examination October 6, 1910. Hysterectomy had been done three years before for gradually increasing dysmenorrhea. Patient had improved greatly in health following this operation. Her symptoms at time of examination in our clinic were of eighteen months' duration. She had an irri-

tating cough and pain in the chest. At first a burning sensation



Fig. 282.—Case No. A35026. X-ray 8086. Mrs. W. R. J., aged twenty-nine. Examined in 1906, when patient complained of lump in left side of neck and pain up left side of the neck to eye and down the left shoulder. Stated that arm swelled, but there was no swelling at the time of examination. X-ray showed bilateral ribs. Operation deferred until March 10, 1910, when left seventh cervical rib was removed. There was marked fulness of supraclavicular fossa, especially the left.

in central lower sternum, which was practically constant and was worse on movement. Within the last six months the pain had

changed somewhat to a "pressure-pain" passing up left side of the neck to a point just beneath the angle of the jaw—sensation of pressure against the neck on the left side. A spasm of the muscle of the throat stopped her in the midst of a sentence; occasionally a feeling as though something were rising up in her throat, as when frightened or excited, and this when entirely free from any emotion. Loss of 29 pounds during the past year. Occasionally had pains shooting down left arm. Physical examination disclosed a little fullness of the left supraclavicular fossa and a bruit which had led to a diagnosis of aneurysm being made elsewhere. There was some tenderness over this area. Patient neurotic. December 10, 1910, a fully developed seventh cervical rib was removed. X-ray did not reveal cervical rib on the right side. There was no sign of aneurysm. This patient had a stormy convalescence following operation. A persistent neuritis down the arm existed for months and is still present to a degree. The cough ceased, the throat spasms disappeared, and she gained more than her normal weight, but is still neurotic.

CASE 30.—A49237. X-ray 11010. J. H. G., male, aged thirty-nine. Examination February 13, 1911. Complained of slight pain on right side of neck, becoming sharp at times on turning head which stretched the muscles on this side. X-ray plate showed bilateral rudimentary seventh cervical ribs. Excision was not advised, but on February 16, 1911, the right side of his neck was subjected to actual cautery and superficial injections of alcohol. He felt sufficiently relieved not to return for excision.

CASE 31.—A71669. X-ray 16589. C. Y., female, aged twenty-one, single. Examination August 6, 1912. Seven years before had noted hard lump on right side of neck. The condition had been diagnosed at that time as a cervical rib, but surgery was not advised, unless symptoms should arise. The patient was nervous and neurotic. Pains down both arms, ache like a toothache over this lump, worse when tired. X-ray showed bilateral seventh cervical ribs rudimentary on the left, complete on the right. Operation August 8, 1912; a complete right seventh cervical rib was removed. Her recovery was uneventful.

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## LUETIC MEDIASTINITIS\*

### A Consideration of Five Cases

H. Z. GIFFIN

Patients presenting the symptoms of mediastinal obstruction become much more interesting as cases for clinical study because of the fact that occasionally their affection may be luetic in character, and therefore more or less amenable to treatment. In general, the treatment of mediastinal disease has been so discouraging that one is glad to arrive at even a tentative diagnosis of syphilis. It is evident, then, that the diagnosis of mediastinal lues may be most important.

In this discussion we have to deal more particularly with chronic diffuse mediastinitis and not with aortitis, aneurysm, or the various forms of tumor. A chronic diffuse mediastinitis may be one of several varieties from a pathologic standpoint. First, and most frequently, it may be due to the extension of a pleuro-pericarditis; second, it may be tuberculous; third, and most important, it may be syphilitic in nature; and, fourth, it may be due to pyogenic or rheumatic infection or actinomycosis.

In the medical literature very few reports concerning chronic syphilitic mediastinitis have appeared. The total number of cases on record is less than 20, but this cannot indicate its proper incidence. Reports of a type of chronic mediastinitis which occurs apparently as an extension of a pleurisy or a pericarditis are relatively common, but these have been rarely syphilitic in character. Dieulafoy has given us the best clinical account of chronic luetic mediastinitis. His description is classic.

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In an excellent discussion of the subject Lian describes in full the symptomatology of chronic luetic mediastinitis, and calls attention to the importance of recognizing the "abortive" forms that cause retrosternal pain, glottic spasm, dysphagia, dysphonia, or give evidence of increased collateral circulation.

A consideration of the reported cases of mediastinal disease would lead one to regard the tentative clinical diagnosis of syphilitic mediastinitis as comparatively simple in most instances. Tumor and uncomplicated aneurysm have usually presented clear-cut features on radiologic or physical examination or both. On the other hand, chronic mediastinitis has been evidenced by a diffuse mediastinal shadow and the absence of the physical findings of aneurysm and tumor. Those cases in which the chronic mediastinitis has been due to an extension of a pleuropericarditis have shown few symptoms of vascular or respiratory obstruction. Those that were tuberculous have shown evidence of tuberculosis elsewhere. Many of those that were syphilitic in nature have shown no evidence of syphilitic lesions elsewhere, and the symptoms of mediastinal vascular obstruction have been most marked.

That a radiologic examination is an essential to the diagnosis of any case in which the symptoms and physical signs seem to indicate the presence of mediastinal disease need hardly be stated. It must be emphasized, however, that a Wassermann test is equally an essential. From a prognostic standpoint one would be almost tempted to dismiss the subject on this basis; that if the radiologic examination show a shadow and the Wassermann reaction be negative, there is, as a rule, little to promise. Should the Wassermann reaction be "strong" positive, there is a considerable chance of improvement, even in the more chronic forms of the affection.

There are, however, details which modify this generalization. For example, if one negative Wassermann test has been obtained, it cannot be concluded therefrom that the affection is not syphilitic. The Wassermann reaction has often become positive after the administration of one dose of salvarsan. It is also possible that a chronic mediastinitis may be present in a syphilitic subject and not be syphilitic in nature.

Moreover, certain complications may be present which render the diagnosis difficult. Sergeant discusses a most important case in which both an aneurysm and a luetic mediastinitis were present, and in which a diffuse shadow in the mediastinum obscured the aneurysm entirely upon radiologic examination. Pulsation, however, was easily seen later when the mediastinal shadow had become thinned out as a result of antisyphilitic treatment.

Sergeant reports another case in which luetic mediastinitis was associated with a gummatous infiltration of the trachea. This patient was seen in extremis and a tracheotomy was done without benefit.

Aside from these rare instances, it would seem that the diagnosis of syphilitic mediastinitis has not been difficult. In the cases reported in which mediastinitis has been associated with stigmata of syphilis elsewhere in the body the diagnosis has been more evident. In those instances in which the mediastinitis is the only evidence of the disease it has been necessary not to neglect the Wassermann test, nor to fail in a thorough review of the history for evidences of infection.

Only a few patients in whom a clinical diagnosis of luetic mediastinitis has been made have come to autopsy. From a pathologic standpoint, therefore, very little is known concerning this condition, and our diagnoses are not absolute. However, the clinical and therapeutic tests are probably sufficient evidence for a positive diagnosis. In other words, if a chronic diffuse mediastinal shadow has been demonstrated on radiologic examination, if the Wassermann test show a very strong positive reaction, and if improvement in the patient's symptoms follow specific treatment, there can certainly be little doubt as to the diagnosis even in the absence of pathologic evidence.

It is my chief object at this time to report in a very brief manner for your consideration five cases which have come under observation in the Mayo Clinic during the last three years, and in which a clinical diagnosis of luetic mediastinitis has been strongly suspected. Four of these cases have been seen during the last year.

The first case is an example of the association of mediastinitis

with multiple syphilitic lesions of the bones. Symptoms attributable to the affection of the mediastinum are not recorded.

CASE I.—L. R., A48439, male, aged thirty-seven. Examination January 25, 1911. The patient gave a history of having had gonorrhea, but no history of syphilis could be obtained. He had had what was termed muscular rheumatism since the age of fifteen. Fifteen months before examination he had suddenly thrown his head back and was immediately attacked by a sharp pain in the neck, the movements in the neck muscles at once became limited, and dull pain on motion had continued since then without definite improvement. This was soon followed by a swelling near the elbow of the left arm and soreness and stiffness in both knees, together with enlargement of the clavicles. A Wassermann reaction was positive. In addition to the bone lesions a radiologic examination showed a diffuse shadow in the mediastinum, not, however, causing appreciable obstruction.

There is no doubt in this instance as to the diagnosis of syphilis. There may, however, be some question as to the nature of the mediastinitis. No signs of pericardial adhesions were present, and it is more than likely that the diffuse mediastinal sclerosis was syphilitic in nature. This patient refused to remain for observation and treatment, and has not been heard from three years after operation.

The second case was associated with abdominal lues.

CASE II.—A. T., A83991, male, aged forty. Examination May 9, 1913. A history of syphilis was not obtained. There was a two-years' history of soreness and some pain in the chest and upper abdomen, together with moderate dyspnea. The patient was well nourished and weighed 175 pounds; had lost only 10 pounds in weight. There was no history indicative of gastric disease. Upon physical examination the liver and spleen were found to be moderately enlarged. There was some edema in both arms and enlargement of the veins in the right arm. Increased dulness was found over the mediastinal area. A radiologic examination of the chest showed diffuse mediastinal shadow, which seemed to account for the patient's symptoms of vascular obstruction. The Wassermann test was a very strong positive. A fluoroscopic examination of the stomach was indeterminate, and pyelographic examinations of the kidneys were negative.



In this instance also the diagnosis of syphilis is quite clear. The absence of a history pointing to malignant disease, the patient's good general condition, the two years' history of complaint, all contraindicated the diagnosis of carcinoma of the stomach. Symptoms of mediastinal vascular obstruction were quite definite. This patient improved while under treatment, but has not been heard from recently (six months after examination).

The third case was characterized by symptoms of mediastinal obstruction, particularly those of a respiratory nature, resulting in attacks resembling spasmodic asthma, together with the expectoration of a moderate amount of sputum at one time and an extension of the process into the hilum of each lung.

CASE III.—J. C., A76525, male, aged forty-eight. Examination November 23, 1912. This patient came complaining of spells of coughing and wheezing which had been considered asthmatic. A history of lues was not obtained. The patient had had gonorrhea many years before and had complained of so-called rheumatic pains. His present illness began about two years before the time of examination, with palpitation, dyspnea, and cough on exertion. The cough was especially troublesome while lying down. Upon physical examination dulness was found in the mediastinal area, and also to the right of the sternum, between the second and fifth interspaces. Diminished breath-sounds and possibly some lagging on expansion were noticed on the right side of the chest. There was no evidence of aneurysm. The sputum was negative for tubercle bacilli and actinomyces. Radiologic examination showed a diffuse mediastinal shadow with extensions radiating into the hilum of each lung. There was no evidence of the radiologic appearance of tuberculosis in the lungs. The Wassermann reaction was a very strong positive.

In this instance the diagnosis was probably as nearly definite as can be attained. The patient improved steadily after intravenous injections of salvarsan; he gained 15 pounds in two months, cough and expectoration entirely disappeared, mediastinal dulness and mediastinal shadow became much decreased, and the lungs were everywhere clear. There was an absence of symptoms upon his examination, February 6, 1913.

The two remaining cases were somewhat similar in nature, and

presented a very striking clinical picture—that caused by vascular mediastinal obstruction and so completely described by Dieulafoy.

CASE IV.—W. H., A86288, male, aged twenty-six. Examination June 19, 1913. A history of syphilis was not obtained. This patient came complaining of swelling of the face. Three months previously he had suddenly become hoarse and the following two months the tissues of the neck gradually became moderately swollen and dyspnea progressively worse. A month before examination the face suddenly swelled within twenty-four hours and remained in this condition. The veins over the sternum, shoulders, and arms became distended, and the patient was in considerable distress. Bending forward caused blueness of the tissues and fulness in the head. Exertion became almost impossible. Upon physical examination the patient was found to be very well nourished and there had been no loss of weight. The face, shoulders, upper thorax, and arms were edematous, with a brawny indurative type of edema. Flatness over the mediastinal area was found. There were no physical signs of aneurysm. The radiologic examination showed a diffuse mediastinal shadow and the Wassermann test was a strong positive.

Upon intramuscular and intravenous injections of neosalvarsan the patient's symptoms improved markedly. Edema of the arms and chest practically disappeared, although some swelling and blueness of the face were still present. Three months after his first treatment, however, the patient returned with an enormous quantity of fluid in the right side of the chest. He was very short of breath, but had not the former signs of obstruction to the flow of blood through the vessels. The fluid obtained was clear in character and the Wassermann reaction was a strong positive. He is at present under treatment. The fluid returns, but the patient's nutrition remains good, and signs of vascular obstruction have not again become prominent.

The diagnosis of mediastinal lues may be questioned in this case. The maintenance of good nutrition and the strong positive Wassermann reaction would be considered as evidence against malignancy. However, it may indeed prove to be some other than a luetic form of mediastinal tumor.\*

CASE V.—H. W., A24759, male, aged forty-three. Examination September 15, 1913. This patient gave a history of infection

\* This patient died December 20, 1913. Pathologic diagnosis of sarcoma was made.

at twenty years of age. Four years before examination there had been some complaint of blood rushing to the head and the face getting red and the ears blue. This was variable and not very troublesome. For the last six months the neck had been gradually getting larger and the dyspnea more marked. For two months the voice had been getting weak. The clinical picture was similar to that of the preceding case, though possibly not quite so pronounced. Radiologic examination showed diffuse mediastinal thickening, and the Wassermann test was negative at the time of the original examination. However, on account of the history of syphilis, the absence of knee-jerks, and a sluggishness of the pupillary reflex the patient was placed on specific treatment. Improvement followed, but was not marked. At the time of his second visit, three months after his first treatment, the Wassermann reaction in contrast to the original test showed total inhibition. This patient is also under treatment, and his improvement is only gradual.

These five cases, as has been seen, group themselves into four interesting types: First, a type in which the mediastinitis was associated with syphilitic lesions in the osseous system; second, one in which it was associated with abdominal lues; third, that in which the process seemed to assume a more subacute form, with expectoration of rather large amounts of sputum, probably from the mediastinum, and in which the clinical picture simulated spasmodic asthma; and fourth, in which two cases gave the very striking clinical picture, so easily recognized, of mediastinal vascular obstruction.

These cases have been presented chiefly on account of their interest from the standpoint of diagnosis. As our experience increases it becomes more and more evident that many obscure affections have in reality a syphilitic basis, and the aphorism that a thorough knowledge of syphilis means a knowledge of medicine acquires greater significance.

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## OBSERVATIONS ON EMPYEMA\*

E. H. BECKMAN

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Musser,<sup>1</sup> reporting on cases of pneumonia from the University of Pennsylvania Hospital, found 9 cases (1.8 per cent.) of empyema in 489 cases of pneumonia. From the literature he collected 12,892 cases of pneumonia in which empyema developed in 276, or 2.1 per cent. In a review of autopsy records he noted that empyema had been present in 5.1 per cent. of 973 cases of pneumonia. These figures illustrate the relative frequency of the complication in this disease.

A disease so common as empyema must be observed occasionally by every general practitioner, and, as I hope to demonstrate, the general practitioner can do the most for these unfortunate patients. Having seen a number of late and neglected cases of empyema, and being obliged to perform some of the severe and mutilating operations for their relief, is my excuse for presenting this subject.

By the term empyema is meant a purulent effusion or a collection of pus in the pleural cavity. The infection may occur after an effusion has already taken place, or the fluid may be purulent from the start. The smaller localized empyemas probably occur in the latter way, and are usually located between the lobes of the lung or at the base of the lung, between it and the diaphragm.

Recent experimental work seems to show that interference with the normal circulation in the pulmonary tissues retards the absorption of fluids from the pleural cavity both by the blood-ves-

\* Read before the Southern Minnesota Medical Association, Owatonna, August 5, 1913. Reprinted from the St. Paul Medical Journal, November, 1913, pp. 533-537.

sels and the lymphatics. This indicates that congestion of the lung in pneumonia favors the collection of fluid in the pleural cavity and retards its absorption. We know that a stagnant accumulation of fluid anywhere in the body, unless formed within its own membrane, such as a cyst, soon becomes infected from the bacteria in the circulation.

Hippocrates recognized empyema and gave explicit directions for the treatment, viz., a free incision down to the rib, trephining of the rib, and incision of the pleura with the cautery or knife. This sound advice by the father of medicine was later neglected or lost, and for many centuries aspiration was the accepted treatment. It may be that the invention of the aspirating syringe by Galen was responsible for this. At least it was considered dangerous to admit air into the pleural cavity. The double fear of sepsis and the entrance of air into the pleural cavity prevented free incision for empyema until the time of Lister.

As an illustration of the results obtained by aspiration in the treatment of empyema I will quote from Paget in his work on "Surgery of the Chest": "For example, as late as 1872 M. Bouchut published, as an instance of good, profitable surgery, a case of empyema in a boy, aged nine, cured in sixteen months after 58 punctures. In another case he punctured the chest, in eleven months, 123 times. Lilly records a case in which he made 56 punctures. Gimbert, in a child eleven years old, made 74 punctures in nine months. And the worst of it all is, out of 48 patients thus tormented, only 6 were saved. Out of 12 patients under the care of Velpeau, not one recovered; out of 58 under the care of Dupuytren, all but two died; and Sir Astley Cooper complained that he could never get a single cure." With this knowledge before us, it hardly seems advisable to accept the advice of one of our present-day surgeons to revert to aspiration and the injection of formalin and glycerin for these cases.

A knowledge of the true pathology of empyema shows us that as soon as there is an accumulation of purulent material within the pleural cavity, either local or general, nature regards it the same as an abscess in any other part of the body, and at-

tempts to limit the absorption by walling it off. In the large collections of pus in the pleural cavity, the walls of this abscess are composed of the parietal and visceral pleura, upon which has been deposited a large amount of fibrinous material which coagulates and later organizes. In operating on some of the late cases one is surprised at the thickness of this limiting membrane, which is often from one-half to nearly one inch in thickness. As the fluid accumulates in the pleural cavity the unyielding wall of the thorax prevents expansion in this direction, so that room is found for the accumulation by compression of the lung. The lung is gradually compressed, and finally retained in this position by the thick limiting membrane of the abscess before mentioned. There are at times many pockets of pus separated from each other by firm walls of adhesions resembling a multilocular cyst, instead of one large abscess. If the empyema has continued for any considerable length of time, this membrane is so resistant that the lung cannot reëxpand after the fluid has been allowed to escape by free incision. It is evident then that, if free drainage be established before these adhesions form or before they become firm enough to hold the lung in a state of collapse, the lung would quickly obliterate the cavity and the patient be rapidly restored to health. This corresponds exactly to the results obtained with free drainage in the early cases. It should be remembered that empyema is not a disease of the lung, although pulmonary disease and empyema may exist at the same time, and that the pulmonary tissue is only slightly or not involved at all in the inflammatory process in a very large majority of the cases. The lung is simply compressed and prevented from expanding by a wall of firm adhesions. The pulmonary tissue retains its power of expansion to a wonderful degree after being compressed for months.

I will report, in a later paper, results in a case in which the entire lung reëxpanded after being totally collapsed for two years. Personally, I believe that the only cases of empyema in which the pocket does not become obliterated after free drainage are those in which the evacuation of the abscess has been delayed so long that adhesions prevent the reëxpansion of the lung. All surgeons

who have had much experience with these cases seem agreed upon this point. If this be true, our duty is earlier operation, with a free incision large enough to break up at the time of the primary drainage the adhesions which are binding down the lung. In order to obtain these cases for treatment before they become chronic the medical profession should know these facts; they should diagnose their cases earlier, and insist on early operation. I wish particularly to call attention to the necessity for early recognition of these cases and an early resort to operative procedure. The internist deserves little credit for sending to the surgeon a patient with a chest full of pus.

Musser states that the diagnosis must be made in part from a full understanding of the antecedents of the infection. Just as with peritonitis, empyema undoubtedly does not occur idiopathically. Pneumonia is the antecedent condition in a large majority of cases. Typhoid fever and scarlet fever are the two other common antecedents of empyema. In the recognition of small empyemas we have chiefly to remember the relationship between pneumonia, other infections and this secondary infection, and therefore to be on our guard if the development of the general phenomena of infection occurs or persists after the pneumonic or other infectious process has apparently subsided. There is such a condition as unresolved pneumonia. I recently explored a chest in a patient having the classic signs of empyema five weeks after pneumonia and was surprised to find that the lower lobe of the lung showed complete hepatization as contrasted with the normal lobe above it. Although there may be an unresolved pneumonia, the condition is more apt to be an empyema. A leukocytosis persisting after the crisis and associated with the general phenomena of infection should warn us that there is a probable focus of pus. Pain continuing after the crisis in pneumonia in a certain localized area, although it may not be severe, and accompanied by a septic temperature, almost surely indicates a localized empyema. The localization of the pus can often be determined by the pain and localized tenderness on the chest-wall.

The aspirating needle is often of the utmost service in arriv-

ing at a correct diagnosis. While many writers warn us of the dangers that may occur from introducing a needle into the pleural cavity, I believe that more good in the way of arriving at an early diagnosis is to be gained from its use than the dangers that may come from a late recognition of empyema. Personally, I have never seen any serious accident come from the use of the needle. In serous effusions which have not become purulent the relief of pressure obtained by aspiration of a portion of the fluid often brings about a rapid absorption of the remainder.

A Roentgen picture of the chest is of the utmost value in arriving at a correct diagnosis in obscure cases. However, it is often an extremely difficult and sometimes an impossible task to determine what the picture shows. One must keep in mind that it is the reproduction of a shadow and that a thickened pleura may cast as dense a shadow as an accumulation of fluid.

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## DECORTICATION OF THE LUNG FOR OLD EMPYEMA\*

E. H. BECKMAN

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One of the most distressing diseases with which the medical profession has to deal is the old case of empyema with a fistula which does not heal. In this discussion I shall consider only the neglected case with a fistula, and not the acute type of empyema. Acute empyema requires an entirely different method of treatment from that given the chronic type with a fistula. Empyema is *per se* a disease of the pleura and not of the lung, although the lung and pleura may be affected at the same time. It occurs more often as a complication following acute infection of the lung.

In studying the pathology of chronic empyema one should consider the disease as an acute abscess occurring in the pleural cavity. Here, as in other parts of the body, nature endeavors to prevent absorption by building up a limiting membrane or wall about the abscess. In the ordinary abscess occurring in the soft tissues this wall is composed of leukocytes, fibrin, and coagulated lymph. In empyema the limiting membrane is the thickened pleura upon which is deposited coagulated lymph, which later organizes and makes a thick fibrous capsule covering both the visceral and parietal pleura. One is surprised in operating on these cases to discover that this membrane is often of extreme thickness, sometimes reaching nearly an inch.

In acute empyema the fluid may accumulate in a short time, the unyielding chest-wall prevents expansion outward, and room is obtained by compression of the lung. If free drainage is es-

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tablished early in the disease, the lung reexpands quickly, thus obliterating the abscess-cavity, and the patient goes on to rapid recovery. In the neglected case, in which the fluid remains in the pleural cavity for a considerable length of time, the lung is compressed so long and the pleura becomes so thick and fibrous that, even after free drainage is established, the lung cannot reexpand. In nearly all cases this is due to the adhesions and not to any disease of the lung. In such a case a large cavity remains in the thorax lined with this unyielding membrane, which covers both the parietal and visceral pleura. The ribs prevent the wall of the chest from dropping in, and the adhesions and the thickness of the pleura prevent the lung from reexpanding. The result is a large cavity which continues to discharge varying amounts of pus. Nature cannot obliterate this cavity, as she ordinarily obliterates abscess-cavities, by collapsing the tissue about it, neither can she force granulations through the fibrous wall of the abscess.

Various methods have been devised by surgeons to obliterate this cavity. In the Simon-Kuster operation, as modified by Estlander, the ribs are resected subperiosteally over the entire cavity. The number of ribs resected varies with the size of the cavity. It is important to be radical and to resect one rib too many, rather than one too few, in order that no dead space remains in the upper or lower part of the cavity to continue supuration. In some cases the pleura is so thick and unyielding that, even after this procedure, it is resistant enough to prevent the wall of the chest from collapsing.

Many surgeons have modified this operation—for example, Wagner, Beck, Quénu, and Tietze, who resected small portions of the ribs through parallel and vertical incisions over the region of the cavity. Jaboulay and Leymaria divided the sternal attachment of the first to the seventh rib, and Boiffin recommends resection of the ribs close to the vertebral column, making use, as it were, of the mobility of the costal cartilage. Recently I saw Wilms of Heidelberg resecting a couple of inches of several ribs along the spine and also along the sternum.

Schede noted that some empyema cavities did not heal even

after extensive rib resections. He also noted that the thickened pleuræ did not unite with each other and directly impeded recovery. Consequently, he devised the operation which bears his name. The procedure consists of removing not only the ribs covering the empyema cavity, but also the thickened pleura and the intercostal muscles, so that the skin and superficial muscles rest directly against the thickened visceral pleura. This operation is usually performed through a U-shaped incision beginning along the external margin of the pectoralis major muscle to the lower part of the thorax, and then backward and upward to the median line of the scapula. The operation is severe, and the shock to the patient is often alarming, if not fatal, especially so since many of these patients are in an extremely weakened condition.

In 1893 Fowler, operating on a woman thirty-five years of age who had had an empyema with a fistula for ten years, dissected out the scar-tissue surrounding the fistulous tract and removed the entire mass of fibrous tissue from the diaphragm and lung. He was surprised to discover that the lung began to reëxpand as soon as this thick scar-tissue was peeled from it. The patient recovered from the operation, and the wound healed entirely within a few weeks. This case was reported in December, 1893. In commenting on the case Fowler stated that the history suggests a method of dealing with some of the instances of old empyema with persistent sinus which resist all the means usually employed for their cure.

Delorme, after observing autopsy cases of old empyema, decided that the lung would reëxpand if the thick membrane was removed from it. Consequently, he devised the same operation, *i. e.*, of removing this enormously thickened membrane from the lung, and reported a case about three months later—in the early part of 1894. Unfortunately, his patient died from hemorrhage and shock.

This procedure, which is called "decortication of the lung," has not received the attention from American surgeons which it deserves. I have been able to find only 24 cases reported in the literature by three operators. The lung's capacity to reëxpand,

if given an opportunity, has not been fully appreciated, and apparently this possibility was not considered by surgeons until the reports of Fowler and Delorme were issued.

Ransohoff, following the work of these two men and appreciating the difficulty of removing this thickened pleura in some cases, advised making multiple incisions at right angles to each other, about a quarter of an inch apart through this thickened pleura down to the lung, so that the entire visceral pleura is gridironed. This is a valuable procedure, and can often be used with good results in conjunction with the decortication process. As an evidence of the lack of appreciation of the opportunity for the lung to expand, Keen states that, as a rule, satisfactory results cannot be expected by this method if the operation is undertaken after four or five months have elapsed since making the primary drainage.

Von Bergmann tells us to remove the costal pleura when it is tuberculous or calcified, or interferes with the recovery of the patient on account of its thickness and density, and also to try decortication of the lung when other methods fail. If it is possible for the lung to reëxpand in a reasonable proportion of these cases without more danger to the patient than by other methods, we accomplish everything that is accomplished by the other methods, and, in addition, restore to the individual a lung or portion of a lung which would otherwise be useless. This factor certainly seems important enough to be considered seriously. From the experience with this method in the Mayo Clinic, our advice would be to try decortication and, when it fails, to try other methods.

Beck injected bismuth paste into sinuses in order to outline them for *x*-ray pictures, and discovered that some of the sinuses healed after this injection. As a result, the paste, which is now made up of one-third bismuth subnitrate and two-thirds vaselin, heated until it becomes a liquid, and, injected as a liquid, will at times heal sinuses that resist other methods of treatment. This paste has also been used for persistent sinuses following an empyema of the chest. Undoubtedly some of the smaller cavities can be healed in this way. Ochsner has reported some very grati-

fyng results by using the method. Our results have not been very satisfactory. If the cavity is of large size or the walls extremely dense, it is difficult to see how it can be obliterated by filling with this bismuth paste.

The writer knows of one case of empyema in which there was almost a total collapse of the lung which had been injected for two years by the discoverer of this method with no improvement. Such a case is not, in our opinion, a suitable one for the method. As previously stated, the ability of a collapsed lung, even after many months, to expand when this thick membrane is removed from the pleura is almost beyond comprehension. In the large cavities, if one has resected several ribs in order to get exposure of the entire cavity, an incision is made through the thickened pleura down to the lung. If the incision penetrates to the lung, a line of cleavage can often be obtained so that large areas, if not the entire pleura, may readily be peeled off. Particular care should be taken to free the area where the lung approximates the thoracic wall in order to free the edges of the lung as much as possible. If the patient coughs or strains during this procedure, the lung in almost every instance bulges into the wound to such an extent that it must be pressed back out of the way in order to continue work. If the membrane is not readily stripped, portions of it may be cut away, and where it is extremely adherent, the Ransohoff method of slitting may be added to the decortication process. This method may also be used about the margins of the lung in order to make them more movable.

In three instances we have removed this thickened pleura from an entire lung in an adult.

CASE 1.—A42485. Male, aged forty years. Three months following a right-sided pneumonia an empyema was discovered and drained. This drainage continued for six months. When the patient was first seen, he was very much emaciated and weakened, and had a persistent cough with a completely collapsed lung on the right side. In November, 1911, the thickened membrane covering the entire lung was removed. The patient suffered considerable shock, but there was very little hemorrhage during the operation.

The lung bulged freely into the wound, and for the first two weeks seemed to fill the entire cavity. Then the patient began to run a temperature, and after several days there was a large increase in the amount of drainage, with relief of the symptoms. The drainage continued until March, 1912, when an exploratory operation was performed, which showed that the lung had again collapsed, and a partial Schede operation was performed to obliterate the pocket. The sinus is still discharging at the present time.

This patient undoubtedly had a collection of fluid form in the pleural cavity two weeks after the decortication, due to insufficient drainage. In our later cases we have placed gutta-percha tissue drains so that the entire cavity may be drained from a single dependent point, and thus prevent the accident which I believe occurred in this case.

CASE 2.—A31028. Male, aged twenty years. Patient had had typhoid fever. He was sick for three months following the typhoid, when an empyema was discovered and drained. This was in January, 1908. The sinuses healed in May of the same year, but began to discharge again in March, 1909, and had been draining until November, 1911, when he came to the Mayo Clinic. Examination revealed a nearly collapsed lung on the right side, with an enormous cavity which had been draining for twenty months. Through an opening large enough to explore the entire cavity the thick fibrous pleura over the entire lung was removed. There seemed to be a number of fibrous bands which entered into the tissue of the lung and seemed to prevent it from expanding. At the time of the operation there were also a great many adhesions between the lower lobe of the lung and the diaphragm which could only be partially freed.

This was considered a very unfavorable case after the operation was finished. To our surprise, however, the drainage stopped entirely on January 5, 1912, fifty-one days after the operation. There were good breath-sounds over the entire lung, the patient has gained 25 pounds in weight, and has remained well to the present time.

CASE 3.—A77103. Male, aged twenty-three years. Was shot in the left chest from in front October 5, 1912. The bullet

passed entirely through the thorax, and was found lodged under the skin of the back. Three weeks later an empyema was discovered and drained. He came under our observation December



Fig. 283.—Röntgenogram of thorax of Case 2. Showing an almost entirely collapsed lung which reexpanded after decortication.

7, 1912. The left thorax was much shrunken, the patient greatly emaciated, and the entire left lung collapsed. He was advised to return to his physician in order to get in better physical health to undergo a decortication. On June 23, 1913, he returned for opera-

tion. This was six months after the drainage of the empyema. complete decortication of the lung on the left side was made -



Fig. 284.—Röntgenogram of thorax, showing an old empyema with thickened pleura drainage-tube extending into the cavity. Suitable case for decortication.

There was very little bleeding, and although the patient seemed to be weak, there was almost no shock following the operation. Drainage ceased entirely in three months. There were good



breath-sounds over the entire thorax, and the patient had gained 19 pounds in weight.\*



Fig. 285.—Röntgenogram of thorax, Case 3. Showing complete collapse of the left lung, with heart pushed to the right.

In addition to these 3 cases of collapse of the entire lung, we

\* Since writing the article, Case 3 developed a temperature and cough. Exploration showed a small empyema pocket which required drainage. About three-fourths of the lung has remained functioning.

have used the method on several other patients having empyema cavities of considerable size. I shall report only two of them.

CASE 4.—A71074. Male, aged twenty-two years. Patient had a left-sided pneumonia complicated with an empyema which was drained in two weeks and healed in five months. Two months later he began to cough and lose weight. The recurrence of the empyema and a large cavity were discovered at this time and drained. Seven months later the cavity, nearly six inches in diameter, posterior to the pericardium, was explored, and the thick membrane covering the visceral pleura removed. The cavity healed entirely in thirty-nine days.

CASE 5.—A73419. Male, aged eighteen years. The patient had a left-sided pneumonia. Two weeks later an empyema was found and drained. The sinus drained for two years, then closed for about three weeks, when it again opened and drained for two months. At this time he appeared at the Mayo Clinic for examination. At operation a large cavity was found lying to the external side of the pericardium. A portion of the seventh rib was removed, and the thick membrane peeled from the lung and pericardium. The cavity closed in three weeks.

These five cases illustrate the possibilities of this operation. In addition, the patients have their normal lung capacity restored, which cannot be said of any other operation for this condition. In our experience the procedure is not as severe as a complete Schede operation, although it appears much more formidable. Hemorrhage from the denuded lung is not ordinarily severe. In several instances it was extremely slight, and while the lung was injured enough to allow air-bubbles to escape in almost every case, no harm has arisen from such injury and apparently no infection in the lung has occurred.

I do not wish to be understood as saying that this operation is suitable for all cases of empyema with a large cavity, but with the patient in suitable physical condition I believe that it should be attempted before any other operative procedure for obliterating the cavity. It has not produced as much shock as the Schede operation, and with reasonable care can be performed in many instances where the Schede operation was formerly indicated.

But one death occurred in 11 cases in our clinic in which this procedure was used. This patient was physically below normal, and had gone through a severe attack of typhoid fever and measles within the year. A large cavity existed which extended to the mediastinum with a connection into a large bronchus. I believe that in this case the operation was carried too far or that the patient received a shock from too much manipulation along the pneumogastric nerves.

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## THE OPERATIVE TREATMENT OF TUBERCULOSIS OF THE SPINE\*

M. S. HENDERSON

Tuberculosis of the spine, or Pott's disease, is of more common occurrence than tuberculosis of any other bone or joint in the human body. Its prognosis is more grave than a like condition in any other situation in the body. This fact does not appear strange when we consider the extremely important function that this flexible bony column performs for us, its close relation to vital organs, and the inaccessibility to attack of the diseased area.

In Pott's disease the body of the vertebra is involved. The large vessels are located in front of these bodies: In the thoracic cavity, the mediastinum, and in the lumbar region the abdominal contents are similarly located. Behind the body, inclosed in its canal, is the spinal cord. Emerging from the sides just behind the bodies are the nerve-trunks. Thus we have a diseased area surrounded by extremely important organs, in which radical excision of the tuberculous focus is forbidden. We must, therefore, confine our treatment to more conservative measures. With the generally accepted methods of procedure and the patient under the best of care, the treatment has not, as a whole, been satisfactory. This is especially true of the ambulatory treatment, which, for various reasons, is the method of choice among American surgeons. Recumbency on the gas-pipe frame is a method which has usually been confined to patients showing symptoms of pressure on the cord. Different appliances are required for the cervical region

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and for the dorsolumbar regions. The varied ingenious braces which have been devised but accentuate the fact that the results have not been all that could be desired.

Briefly, the end to be attained in the treatment of these cases is to throw the weight on the posterior portions of the vertebra until the disease has run its course and ankylosis occurs. To give such support and provide absolute fixation by the use of external appliances, such as plaster jackets or braces, is mechanically impossible. Particularly is this true in the thoracic region, where respiration produces constant slight motion. Lange and others attempted to overcome this motion by splinting the spinous processes and laminae together over the site of the disease by the use of metal plates, etc. This was not satisfactory, however, and has been quite generally abandoned. It would seem wise, therefore, to view with great favor any operation or procedure which will tend to bring about a cure of the disease before there is advanced destruction of the bodies of the vertebrae.

The cure of tuberculous joints by the production of ankylosis has been rather forcibly brought to our notice by Ely's work during the past two years. He explains his results on the ground that the tubercle bacilli thrive and multiply in the spongy or cancellous tissue at the epiphyseal ends of the bone. Stiles and various other observers have called attention to the frequency with which tuberculosis was encountered in the metaphyseal area.

It was formerly taught and believed that the primary focus in tuberculosis of joints was rarely in the synovia. Ely firmly contended that the synovia was generally the soil first attacked, and this opinion is gaining ground. In the cases observed in the Mayo Clinic this evidence has been corroborated as nearly as it can be by clinical examinations, the use of the *x*-ray, and the findings at the operating table. The cases selected for resection naturally are in the final stages of the disease and so much destruction has taken place that the primary focus is lost in the final picture.

In affections of the joints we have the *x*-rays as a means

of positively determining if there be erosion or abscess of the bone. A close study of these cases leads one to believe that primary tuberculosis in the synovia is the rule, at least in adults, and the condition should be frequently looked for in children. Stiles notes this point in one of his recent papers on the subject and says that the majority of his cases (in children) of tuberculosis of the knee were primarily synovial.

The particular point made by Ely is that in a resection of a tuberculous joint the function of the joint as such is brought to an end. Ankylosis occurs, and the character of the concerned epiphyses is gradually altered from spongy bone to that of hard compact bone which is characteristic of the shaft.

Rarity of tuberculosis in the shafts of the long bones has long been noted. In the area previously occupied by the diseased joint we find a gradual change of soil from one favorable to the lodgment and growth of tubercle bacilli to one distinctly unfavorable to the growth of the bacilli. The result is a gradual elimination of the tuberculosis practically by starvation. This process is perhaps best illustrated by considering what occurs after resecting a tuberculous knee-joint. The tibia and femur gradually unite into one long bone. In some instances it has been shown that the medullary cavity of the one becomes continuous with that of the other, resulting in one long bone from hip-joint to ankle. Radical removal of all the diseased tissue is not practical and it is clinically well known that in these resections much tuberculous tissue is left in the soft parts. If enough of the surface of the joint be removed to bring about an ankylosis, the disease will disappear, the ankylosis and consequent arrest of function bringing about a cure.

The pathology of Pott's disease is similar to the pathology of tuberculous joints elsewhere in the body. The spine is a column composed of many vertebræ and consequently many joints. Anteriorly it is made up of the bodies of the vertebræ, which are composed of spongy bone, synovial membranes, and intervertebral cartilaginous discs. The posterior portion of the spine is made up of the transverse processes, laminæ, and spinous processes—all

composed of hard bone. It follows, therefore, that the anterior portion of the spinal column is the soil most favorable for the development of the tubercle bacilli.

Whether or not the disease be primary in the synovia or in the bone is not of practical importance in Pott's disease. A radical excision cannot be done advantageously as it could were the disease in the knee-joint, and we must, therefore, wait for the curative ankylosis which occurs slowly and tediously by the disintegration and absorption of the synovia and cartilaginous discs. During this time more destruction of bone takes place, causing a greater deformity, which deformity appears immediately posterior to the diseased vertebræ, its contour depending upon the number of vertebræ involved and the extent of the disease.

Postmortems have been made on individuals who some time during life had had Pott's disease from which they recovered. In some of these individuals a firm ankylosis had occurred between the laminæ of the affected vertebræ and also between the spinous processes. The whole of the posterior portions of the vertebræ were firmly fastened together. It has been deduced that the cure of the disease was brought about by the absolute fixation thus rendered. This deduction is in accord with the cure of tuberculous joints elsewhere in the body. If by operative interference we can hasten the ankylosis, much will be accomplished toward the cure of the patient.

Hibbs has published a paper in which the above point is emphasized. He describes his technic for an operation and reports some cases. Albee has also reported some cases and described the technic of his operation. Hibbs has not made use of the transplant, whereas Albee takes a wedge-shaped piece out of the tibia and lays it between the split spinous processes. The object of both operations is the same, *i. e.*, the formation of a strong posterior splint to prevent absolutely any movement of the diseased portion of the spine.

The technic of the Hibbs operation is as follows: The patient is placed in the ventral position. "A longitudinal incision is made directly over the spinous processes through the skin,

supraspinous ligaments, and periosteum to the tips of the spinous processes. The periosteum is split over both the upper and lower borders of the spinous processes and the laminæ and stripped from them to the base of the transverse processes." The spinous

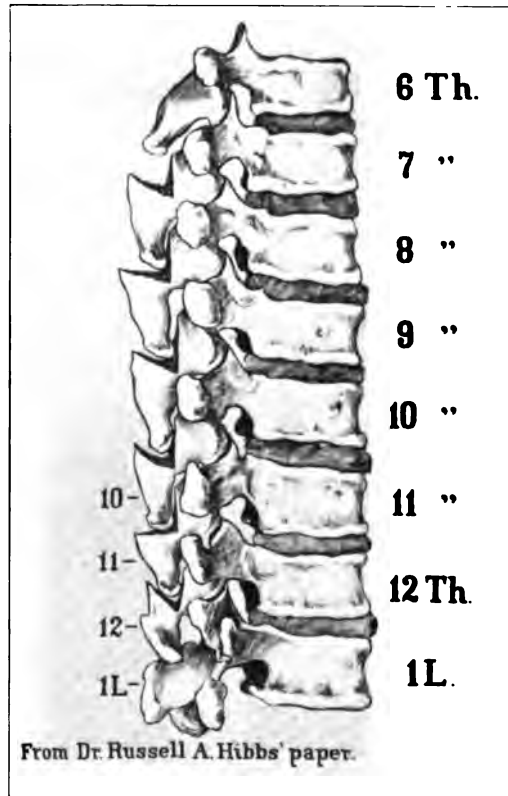


Fig. 286.—Diagrammatic representation of the Hibbs operation, showing the method of fracturing the spinous processes near their base and pressing the tips down on to the surface of the raw bone.

processes are then subjected to a green-stick fracture near their base, about three-fourths through their upper and lower diameters. The tips are then pressed downward to repose in the denuded area caused by the fracture of their fellow spines below. This is repeated with three or four spines above and below the



kyphos. An effort is made to secure ankylosis of the laminae, the advantage of which is obvious, for, instead of having an ankylosis of only the spinous processes, the entire posterior surface of the affected vertebræ and two or three vertebræ above and below will be grown together. They will be immovable one on the other. By this broad ankylosis any tendency to rotation or rocking will be prevented. To obtain this condition the periosteum is pushed back well on the lateral processes and a chip of the lamina from the upper vertebræ is raised and bent downward, without completely severing its connection from the lamina to the lamina of the vertebra below. "The lateral walls of the periosteum and of the split supraspinous ligaments are brought together over these processes by interrupted chromic catgut sutures. The skin-wound is closed and a steel brace applied with the space between the uprights increased somewhat at the site of the wound so as not to make pressure on it. Rest in bed is absolute for eight weeks. During the next four weeks sitting up is permitted; at the end of the twelfth week walking is allowed. The brace is continued for another month, when it is removed for a part of each day until gradually it is left off entirely."

The following technic for the transplantation of bone is used by Albee: The patient is in the ventral position. A curved skin incision a little to one side of the median line is made and the tips of the spinous processes exposed. With a chisel the spinous processes and the interspinous ligaments are split longitudinally to a depth of about three-fourths of an inch. This is done to all the diseased vertebræ and to at least one healthy one on each side of the diseased area. The gutter for the transplant is now ready, and a hot saline pack is placed in the wound. With the patient still in the ventral position the leg is flexed on the thigh, a sand bag placed in the popliteal space, and an incision made over the crest of the tibia. A wedge-shaped piece of bone of the desired length is removed and placed in the gutter formed for it. Care must be taken in the removal of this piece of bone that too much force be not used. The wedge should be secured by chisel-

ing carefully on both sides of the tibial crest. If the attempt be made to remove it by chiseling only one side of the crest and sawing transversely, at each end too large a piece will be removed, thus weakening the tibia. The piece of bone is firmly tied in



Fig. 237.—Diagrammatic representation of the placing of the bone graft in the gutter formed by the split spinous processes. Note the method of splitting the spinous process so as to leave a firm lever for the graft to adhere to.

place and the incision closed. Postoperative treatment: The patients are placed in the recumbent position on a gas-pipe frame or a fracture-bed from five to twelve weeks, after which they go about without apparatus.

The technic of Hibbs and of Albee in their respective operations has been adhered to in the main in work done in the Mayo Clinic, except when for various reasons minor changes have been made to suit the individual case. The recumbency has been insisted on following operations, but patients have also been required to use the brace longer as a precautionary measure. These operations promise to be of great aid in the treatment of Pott's disease. In applying the procedures to young children we do not know what the effect will be on the growth of the spine. The transplant or ankylosed posterior portion may not grow apace with the anterior portion, but it must be remembered that the anterior area may be so diseased that the growing centers are destroyed. This is a problem that time alone will clear up, and the operation need not be forced until this point is clear. Children are more easily treated on the Bradford frame than adults. There appears to be no objection to the operation for adults.

The operation in itself, either by the Hibbs or the Albee method, is simple and attended with practically no risks. A rigid aseptic technic is most essential. The operation is not ideal, as one would prefer to attack the diseased anterior portion of the vertebræ. The splinting of the bodies would be the ideal operation mechanically, but anatomic structures forbid such interference so we must be content with the posterior portion of the vertebræ, which at any rate nearly always is clean and suitable for plastic or transplantation work.

Thirty-five patients with Pott's disease were referred to our clinic during the year 1912. Twenty-eight in this series were males and seven were females. Age of the oldest, fifty-two; age of the youngest, three; average age, twenty-four years. For various reasons only six of these patients were submitted to operation. Some were rejected because of advanced phthisis, posterior sinuses too near the site of the operation, amyloid degeneration, etc. The Hibbs type of operation was used in three of these cases, the Albee in three. There were five males and one female in the series. The age of the oldest patient operated on was forty-two years and of the youngest, three years. The results to date in these

six cases are encouraging, but the time which has elapsed is too short from which to deduct definite data. Following the operation these patients were treated by the reclining position on the Bradford frame from four to eight weeks, after which a Taylor brace was worn. This brace is considered very essential. All the ordinary dietetic and tonic methods of treatment were carefully carried out.

Neither the acuteness of the condition nor the presence of an abscess, providing it points at a sufficient distance from the field of operation, need contraindicate operative procedures in these cases.

CASE I.—A62441. E. F., male, aged four. Examination December 20, 1911. Indefinite history of weak back since beginning to walk. Five months before the patient came for examination the mother noted "lump" in back. He was fairly well nourished, walked with spine rigid, head thrown back, and could not bend over to pick anything off the floor. Walked very little and rested his elbows on chairs wherever possible, to support back. Reflexes exaggerated. Well-marked kyphos at lower dorsal and dorsolumbar juncture. Treatment on Bradford gas-pipe frame and casts was recommended and carried out until August 1, 1912, a period of eight months. The deformity increased and paralysis (not complete) set in. August 10, 1912, a modified Hibbs operation was performed on the tenth, eleventh, and twelfth dorsal, and the first and second lumbar vertebræ. Wound healed by first intention. Recumbency treatment on the frame was then carried out for three months, after which a Taylor back-brace was applied and walking gradually encouraged. On January 15, 1913, the patient was dismissed, wearing a brace and walking everywhere with comfort. Gait normal. Reflexes normal. Well nourished and healthy in appearance.

CASE II.—A63801. M. R., male, aged three. Examination February 5, 1912. Patient first complained of back in October, 1911, although parents had noted lump in back three months previously. The lump, which was a well-marked kyphos at the dorsolumbar juncture, steadily increased in size. X-ray showed distinct involvement of the twelfth dorsal vertebra, with lateral deviation to the right at the dorsal lumbar articulation. The child walked very little and then only by leaning his hands on his bent knees

and waddling about. Patellar reflexes were exaggerated. He cried at night and had a daily temperature of 99° F. to 100° F. in the afternoon. He was placed on a Bradford frame and kept there for six months, after which walking was permitted with a Taylor back-brace, but he did not walk well and the symptoms were renewed. The parents then desired to have the operation performed and the Hibbs type was selected. Operation, September 7, 1912. The tenth, eleventh and twelfth dorsal and the first and second lumbar vertebral spines were dealt with according to the technic previously described and the usual after-care carried out. A letter from the mother dated January 30, 1913, states the child is walking very well and is perfectly comfortable and has grown taller. The lump remains the same. The patient will be brought to the clinic for examination in the spring.

CASE III.—A70330. E. F., male, aged twenty-three, single. Examination July 9, 1912. This patient had had constant pain for two and one-half years in the left lumbar region, around left side to front of abdomen and into left testicle. At times this pain keeps him from bending his back and makes walking difficult. No vomit, no fever. Had not been able to work the preceding winter and spring. Lost 10 pounds in weight in two years. No gastric complaint. Bowels fairly regular. Urination normal. Had noted lump in his back December 25, 1911. Physical examination showed patient fairly well nourished. A mass, evidently a psoas abscess, filling practically the whole left side of the abdomen, was palpated. There was a slight kyphos at the second lumbar vertebra. Lumbar spine rigid. X-ray showed involvement of the first and second lumbar vertebræ. Afternoon temperature of 99° F. to 100° F. July 17, 1912, the Hibbs type of operation was performed to fuse the last dorsal and the first, second and third, fourth and fifth lumbar vertebræ. Healing by first intention. The patient was kept on the gas-pipe frame for one month, then provided with a brace and sent home for two months. When he returned the psoas abscess was even more prominent than before. On November 27th the abscess was opened, drained, swabbed out with 3.5 per cent. tincture of iodine, and the wound sewed up. Wound healed by first intention. The kyphos was practically gone. A letter from the patient dated February 5, 1913, states he is feeling fine. Still wearing brace, but wishes to discard it. There has been no return of the psoas abscess. He was advised to continue the use of the brace for two months longer and then to report again.

CASE IV.—A73969. J. K., male, single, aged forty-two. A prospector from Alaska. Examination on September 23, 1912. At seventeen years of age he had been treated for one year for Pott's disease. A deformity, though slight, was present from this time on. There was always slight weakness in the back, though he was able to follow the hardy existence of a prospector. Had had gonorrhea, but not syphilis. In March, 1912, while being drawn to the surface of a mine, the rope broke and he dropped 60 feet. Left forearm broken and back injured. Delirious for two weeks. Kyphosis at ninth and tenth dorsal vertebræ much increased since the accident. The fracture healed in bad position and the left shoulder remained stiff. He complained of general weakness and could not walk far because of weak back. Constipated, with partial loss of control since the accident. Operation rather than treatment by braces or cast was elected, and the Albee type performed on September 28, 1912. A wedge-shaped transplant about seven inches in length was removed from the crest of the right tibia and placed in a gutter formed by the split spines of the seventh, eighth, ninth, tenth, eleventh, and twelfth dorsal vertebræ and was fixed in place by aid of chromicized catgut. The skin in the scar over the ends of the transplant did not heal readily, but no infection occurred, and in about three months it was completely healed over. (Since then we use a curved incision to one side of the spinous processes so that the skin-wound does not come directly over the field of operation.) The patient was kept on the frame for five weeks, after which the back-brace was applied. Several attempts have been made to discard the brace, but the patient always requests to have it reapplied. He is better in every way but by no means fit to take up the rugged life of a prospector.

CASE V.—A73346. B. B., female, single, aged thirty-four. Examination September 9, 1912. History of pain in back for about nine years. Pott's disease had been diagnosed, and patient was treated with casts, braces, etc., with no permanent relief, her condition growing steadily and slowly worse. She had known of a prominence in the dorsal spine (sixth-seventh) since onset of symptoms. Subject to spells with pains in the arms, legs, and ankles. Pain more severe at night—considerable loss of sleep. She was having "one of her bad spells" at the time of examination. The x-ray was not helpful because of the location of the disease. The principle of the operation was explained to the patient and she decided to take advantage of it. On September 19th the Albee type of operation was performed. A wedge-shaped piece

was removed from the crest of the right tibia and bridged across the split spinous processes of the fourth, fifth, sixth, seventh, and eighth dorsal vertebræ. Both wounds healed by first intention. Recumbency on the frame for nine weeks, then the Taylor brace was applied and walking gradually permitted. A recent letter states that she is free from pain and better than she has been in years.

CASE VI.—A22270. T. S., male, single, aged twenty-three. Examination April 8, 1909. Diagnosis—tuberculous pleurisy (right side). Right tuberculous epididymitis. On April 14, 1909, right epididymectomy was performed. The convalescence was uneventful. December 19, 1912, he again came to the clinic complaining that for the past two years he had had pain of a dull, almost constant character in the small of his back. Worse when moving around. No chills, fever, or sweats; no cough. Had gained in weight. Painless swelling in the left scrotum for last one and one-half years. The x-ray examination of the spine was not satisfactory due to the mediastinal contents with the large vessels being immediately in front of the diseased area. A curved deformity was present in the region of the sixth and seventh dorsal vertebræ. The left epididymis was hard, painless, and enlarged. On December 30, 1912, the Albee operation was performed. A curved skin incision to one side of the median line was made and the transplant placed in the split spinous processes of the fifth, sixth, seventh, and eighth dorsal vertebræ and tied in with four doubled strands of linen. The transplant was taken from the right tibia. The diseased left epididymis was removed. All the wounds healed by first intention. He was kept on the frame for four weeks and is now walking about more easily with a modified Taylor brace on.

The report on these patients is essentially preliminary, but a review of their condition is encouraging. Three of them had been treated by the accepted conservative methods with poor results. Whether the relief afforded by the more radical treatment will be permanent remains to be seen.

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## THE TREATMENT OF MALUNITED FRACTURES OF THE SHAFT OF THE FEMUR \*

E. S. JUDD

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The standard of measurement of the deformity following fracture of the shaft of the femur is the amount of actual shortening of the limb and the degree of eversion or inversion of the foot.

It is very important to obtain a good cosmetic and anatomic result, though it may be difficult because a part of the fractured bone may be absent or broken in such a way that it is almost impossible to approximate the rough and irregular fragments and the torn soft tissue.

A good functional result is by far the most important, and is sure to follow if the anatomic approximation is good. Fortunately, it is obtained in a large percentage of fractures of the shaft of the femur, even though the cosmetic and anatomic results are faulty. Cases are recorded in which good function has resulted after the apparent shortening of an extremity of  $1\frac{1}{2}$  inches. A commission appointed by the Pennsylvania Medical Society to investigate the results of fractures of this kind report findings of a year's work in which the results were considered good even if the measurements showed more than an inch of shortening and provided there was no inversion or eversion of the foot from angulation of the fragments.

Radiography has come into such common use and such good work is being done everywhere that no one with a fracture of the femur should be denied the benefits of treatment to be obtained through a careful *x-ray* examination. In a series of over 200 non-

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operated cases carefully examined by Estes, perfect restitution of the fragments was brought about in less than 2 per cent. and yet the functional result was excellent in each case. Estes believes that *x-ray* examinations should be made before and after the reduction and several times during the course of the treatment if necessary. Harris recommends that the patient be shown the *x-ray* findings and that these findings be demonstrated and explained carefully in order that there may be no misunderstanding or trouble in case a perfect result is not obtained. The average shortening in cases of malunited fractures of the shaft of the femur before treatment is instituted is nearly  $1\frac{1}{2}$  inches. The radiogram will demonstrate this more readily and satisfactorily than any other means of explanation.

Because of the location, function, and size of this bone, fracture of the shaft is a serious condition. In a very large percentage of cases good results will follow the conservative treatment, and, if the fragments can be brought into a satisfactory apposition with a reasonable surety that there is no soft tissue intervening, this treatment would seem to be the one of choice.

The arguments for and against the open treatment for fractures of all kinds are well known at the present time, each side having its advocates. On account of the absolute necessity for a firm union in good position of fractures of the shaft of the femur, it would seem best to be less conservative than in most other instances. In my opinion the open operation and Lane plating should be done more often in fractures of this particular bone. It is assumed, however, that the open operation should not be performed except under such circumstances and conditions as would be suitable in any major operation. If the open operation is performed more often in this class of cases, I believe it seldom will be necessary to operate on such cases as are herewith reported.

CASE I.—A59476. Male, aged five. Six weeks before coming for treatment he had fallen from a wagon, sustaining an oblique fracture of the middle third of the left femur. The fracture was reduced and put in the usual dressing. Four weeks after the injury the dressing was changed to a plaster-of-Paris

cast. Examination in our clinic showed a firm union with about  $1\frac{1}{2}$  inches shortening and the foot markedly inverted. The radiogram showed overriding and angulation of the fragments apparently rather firmly united. With this degree of shortening and malposition we believed it would not be advisable, especially in a child of his age, to wait and see how much correction would take place of its own accord and operation was advised. Upon opening through the soft tissues, plenty of evidence of callus and a firm union were found and the bone was re-fractured in the line of the old fracture. In putting extension on the limb it was found that considerable muscular contraction had taken place, so that when quite firm extension was applied, there was a tendency for the fragments to separate and soft tissues to drop between them. It would have required a great deal of force to extend the limb far enough to approximate the fragments accurately and to apply a Lane plate. We believed that slow gradual extension for a few days would in all probability approximate the fragments in their normal position without making too great traction at one time on the nerves and vessels and other soft tissues. As a means of holding the separated fragments together in a manner to approximate the fractured surfaces and yet allow the gradual extension to overcome the muscular contraction until the fragments were accurately approximated, two loops of a moderate sized aluminum bronze wire were used. These were passed loosely around the fragments about three-fourths of an inch apart. The wire was not set tight onto the bone.

If extension is put on as the lower fragment is pulled down, the wire loop allows this fragment to slip through, but as it does so, it draws the two fragments firmly together. After the wire loops have been accurately placed and the soft tissue closed, a regular Buck's extension is applied. The result in the above case at the end of a few weeks was a primary healing of the operative wound, full use of the limb, with no shortening and no visible deformity.

CASE II.—A58588. Male, aged seven. Four months ago the child caught his foot in a rope and was dragged against a stone curbing. He was treated elsewhere in the usual manner for six weeks. Examination in our clinic showed a fairly large callus at the junction of the middle and upper thirds of the shaft of the right femur. There was some angulation, considerable rotation turning the foot inward, and more than one inch shortening. An operation was

performed as described above, *i. e.*, refracturing in the line of old fracture, placing one or two loops of wire so as to include both fragments loosely, closing up the wound in the soft tissues, and the application of Buck's extension. The result in this case at the end of several weeks was firm bone-union in good position, one-quarter inch shortening.

CASE III.—62684. Male, aged twenty-nine. Left thigh and femur had been crushed by a huge rock one year ago. This had caused a double fracture of the femur, one at the lesser trochanter and one in the middle third of the shaft. He had been treated for five weeks, then operated on and wired. A sinus developed, and four months later he was reoperated on and the wires removed. There was no union at this time. One year after the injury he was examined in our clinic. At this time there was no union, fragments were in malposition, with four inches shortening, and there were three sinuses at the site of the fracture in the middle third of the left femur. The motion in the knee-joint was greatly limited. Radiogram showed much overriding of the fragments, several smaller pieces of necrotic bone, and considerable soft callus with no firm union. The operation consisted of a free incision in the soft parts of the outer side of the thigh and cleaning out pieces of necrotic bone and of fragments of the shaft. There was firm union of the fractured parts at the lesser trochanter. Because of the extensive soft callus, it was difficult to discover the exact line of the old fracture. With Gigli's saw this soft callus and a part of the fragments were sawed in such a way as to simulate the condition of an oblique fracture. A loose heavy wire was passed around the two fragments, the soft tissues were closed, and a Buck's extension applied after turning the foot into its proper position. Union in this case was very slow. There was much discharge from the old sinuses for many weeks, but after several months the bone became solid and the patient was able to walk without crutches. Although this patient was up in heavy extension for many weeks, the four inches of shortening was not materially reduced, and considerable limitation of the knee-joint still exists, due, no doubt, to the extended contractures and scars from the discharging sinuses.

CASE IV.—A58885. Male, aged nine. This child had been operated on elsewhere for appendiceal abscess thirteen weeks before coming to our clinic. Convalescence from this operation was uneventful until on the ninth day, while playing on the floor, he

reached forward and felt a sudden snap in the left thigh. He was treated for a pathologic fracture, had had an extension for four weeks, and casts for nine weeks. Examination in our clinic showed a fracture of the upper end of the left femur with  $1\frac{1}{2}$  inches of shortening. The entire leg was markedly inverted, and there was evidence of union between the fragments, though it was not firm. The radiogram showed a fracture through a fusiform enlargement in the upper third of the femur, which was undoubtedly a bone-cyst. Operation in the eleventh week following the fracture showed considerable enlargement of the shaft at this point, and a fracture through the center of the enlargement. There was much soft callus, but no firm union. By means of Gigli's saw the entire soft callus and ends of the fragments were cut through in an oblique direction, and a wire loop placed around the two fragments which had been produced by sawing. The wound in the soft tissue was closed, the malposition corrected, and extension applied. In four weeks there was considerable evidence of bone-union, and at the end of twelve weeks the child was allowed to walk. Measurement and examination at this time showed there was no shortening and that the motions of the joint were normal.

If conclusions can be drawn from these few cases, we may assume that reoperating on malunited fractures of the shaft of the femur can be done satisfactorily, and that we may expect not only to overcome the inversion or eversion, but also a considerable part, if not all, of the shortening. This assumption is, of course, more plausible if the fractures are not too old. I also believe that in certain of these cases the employment of one or more loops of wire insures a good firm approximation of the surfaces of the fragments, without in any way interfering with the lengthening-out produced by gradual continuous extension.

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**TECHNIC**



# A DISCUSSION OF VARIOUS ANESTHETICS AND METHODS

## EXPERIMENTAL OBSERVATIONS\*

BERNARD FRANCIS MCGRATH

The purpose of this paper is, first, briefly to discuss the present status of the question of anesthetics, secondly, to contribute data from the Mayo Clinic, and, lastly, to present some preliminary observations on an experimental work which is to be continued at length.

A stimulus has recently been applied to the question of anesthesia, which has resulted in a wide-spread interest and in laudable endeavors toward advancement. New anesthetics and various combinations have been employed, apparatus aiming at accuracy has been designed, and different routes of administration have been practised. Commendable and seemingly progressive as are all these efforts, still does not their multiplicity itself emphasize the general state of inefficiency that exists?

To enumerate and describe the several anesthetics, devices, and methods which have been advanced would be an unnecessary repetition, since their details are already known, or at least are easily available in the literature. Each has enthusiastic advocates, but which can withstand the test of time?

It has been authoritatively stated that any of the recognized anesthetics or methods is safe in the hands of an expert anesthetist. In an endeavor to place this phase of surgery on an efficient basis should we not begin by investigating the undermost stones in the

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foundation? In analyzing these is not the administrator of the anesthetic one of the first to attract our attention? Embodied in the expert are those qualities which are essential for the successful production of anesthesia. He guards against the use of anesthetics which contain impurities; his extensive experience frequently enables him to obviate deleterious psychic conditions preceding the operation; his skill in administering ameliorates the mental and physical disturbances of the initial stages of anesthesia; he avoids the recognized nocuous effects caused by vacillation between a light and a deep state; and finally, the expert administers the anesthetic only in amount sufficient for the conditions, thereby reducing to the minimum immediate postanesthetic and remote organic effects.

Crile speaks of "two great classes of association, namely, those that are injurious and those that are beneficial. The injurious kind are called 'noci-association,' that is, nocuous or injurious associations." Crile's scientific defense of his theory, together with his and others' observations of its practical application, is sufficiently convincing to demand serious consideration and a general effort to test its soundness.

Although extrinsic to the patient, yet seemingly comprehended in this principle, are certain other "noci-associations" which, until recently, were nearly omnipresent in the hospitals of this country, and even today exist to a culpable degree. I refer to the inexperienced house-officer as the official anesthetist of the hospital, and the indirect detriment which results to the patient through the mental disturbance, and, in consequence, the curtailed efficiency of the operator. The chain of asepsis may be intact, the surgical assistants adequately equipped with skill and discipline, and the surgeon most able; but, with the patient at one period rigid and practically inoperable, the next period assuming an antemortem aspect, the operator must necessarily be incapable of his best effort. Therein an injustice has been done, since the benefit to the patient if the anesthetist be excepted, is not commensurate with the pathologic condition which he presents and the efficiency of his environments.



The best anesthetic administered by the most expert anesthetist would be the ideal in anesthesia. Such an ideal condition is no more feasible than that every surgical operation be performed with the best technic by the most skilful surgeon. The reasons are obvious. That the expert anesthetist is not now and never will be generally available is self-evident, but that there is a vast territory of the medical field in which such idealism could and should be applied the most skeptical will not deny.

It is but truth to state that medical schools in general have not adequately taught and emphasized this seriously important branch

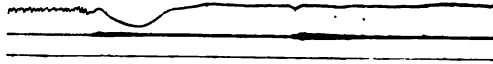


Fig. 288.—No. 635 a. Intravenous ether, 5 per cent. First part of tracing, no anesthesia. Note the result of careful induction and maintenance of anesthesia. Duration, one and one-half hours.

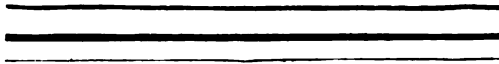


Fig. 289.—No. 635 b. Tracing made at the end of one hour, surgical anesthesia, intravenous ether, 5 per cent.



Fig. 290.—No. 691. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note early effects of anesthetic on cardiac action and respirations and relation of respiratory failure to effect on heart. Spontaneous recovery.

of medicine. In many instances men are graduated with little theoretic and far less practical knowledge of the subject. Just as the student with a bent toward surgery, pathology, or any of the other branches of medicine should be encouraged and scientifically trained in that direction, so, too, should the one adapted to the work of anesthesia be similarly encouraged and guided.

One has but to scan the statistical history of anesthesia to note the wide divergence of results. This diversity seems to be due primarily to a lack of parallelism of all the factors concerned. Some of the obviously essential factors in estimating the comparative

value of anesthetics and methods are the purity of the drugs, the skilfulness of the anesthetist, a reasonable parallelism in the number of cases observed and the condition of the patients.

The comparative value of the anesthetics more recently advanced and the methods of administering them are at present and for some time must remain in the balance.

It is easily conceivable that some of the more recently advocated methods of inducing anesthesia are positively indicated in

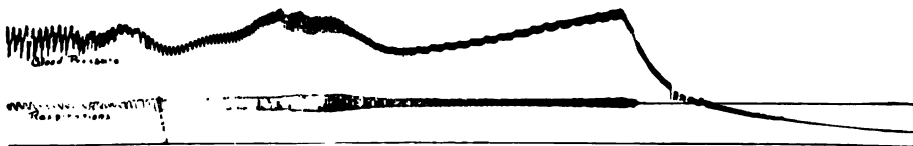


Fig. 291.—No. 677. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note induction of light anesthesia in first and second thirds of tracing. In the last third note effect of "full flow" for twenty seconds (solution, 126.60 c.c.; ether, 6.30 c.c.). No recovery. Heart failed about two minutes after cessation of respirations.



Fig. 292.—No. 615. Intravenous ether, 5 per cent. Showing effect of overdose—"full flow," thirty seconds (190 c.c. solution; ether, 9.5 c.c.). Note continuance of cardiac action (upper line) for about four minutes after cessation of respirations.

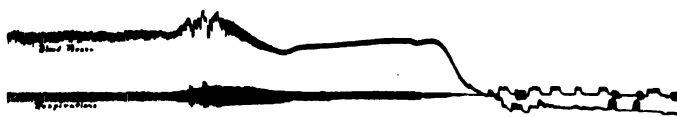


Fig. 293.—No. 675. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note effect of accidental overdose and ineffectual efforts at resuscitation. Total solution, 450 c.c.; ether, 22.5 c.c. Time, six minutes.

some operative procedures, and at least helpful toward efficiency in others. This is particularly true when applied to operations about the head and neck and within the thorax. In this regard the methods of Crile, Meltzer and Auer, and others are particularly applicable. The indications for the intravenous administration of anesthetics seem at present to be very limited, although time and research may radically alter this view.

In making a wide survey of the field of surgical achievements, including statistical history, supplemented by the opinions of keen

and progressive observers, no other anesthetic or method for application in general is so soundly supported by time and experience as ether administered by an expert, with a due allowance of air to the patient. Compared with other anesthetics and methods, ether by the so-called "drop" method is at least as immediately safe, is more available, more economic, and more conducive to



Fig. 294.—No. 672. Intravenous ether, 5 per cent. First part of tracing, no anesthesia. Note induction of anesthesia, practically synchronous cardiac and respiratory failures and ineffectual efforts at resuscitation. Total solution, 300 c.c.; ether, 15 c.c.



Fig. 295.—No. 683. Intravenous ether, 5 per cent. Note relation of respiratory to cardiac failure and the ineffectual efforts at resuscitation, when artificial respiration, heart-massage, and abdominal pressure were begun late. Total solution, 350 c.c.; ether, 17.5 c.c.



Fig. 296.—No. 683 c. Intravenous ether, 5 per cent. First third of tracing shows effects of "over-dose"—ether, 9.4 c.c. in one minute and epinephrin 3 drops; middle third, temporary signs of recovery, with subsequent failure, despite efforts at resuscitation.



Fig. 297.—No. 673 a. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note induction in middle third and effect of twenty seconds' full flow—solution, 126 c.c.; ether, 6.3 c.c.—in last third. Abdominal pressure. Recovery.

efficiency in extensive work. I am not cognizant of data sufficiently reliable and extensive to prove that in the hands of the skillful the immediate deleterious effect on the condition and comfort of the patient, and the remote effect on the organs of the body, are more than those of any other anesthetic or method.

The advancement which is being made in the application of local anesthetics augurs well for substantial aid to surgery along

these lines and this affords a most fertile field for research. General anesthesia is at best a fairly wide deviation from the normal, but, in the present state of our knowledge, is absolutely indicated in many cases. With the scientific advancement of local anesthesia we may hope to see the number of indications for general anesthesia reduced to a minimum.

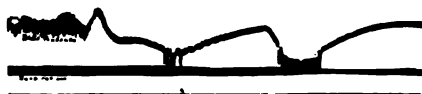


Fig. 298.—No. 693 a. Intravenous ether, 3 per cent. First part of tracing, no anesthesia. Note induction of anesthesia (light). Last of tracing depicts the effects of thirty seconds "full flow," 4.7 c.c. ether, with spontaneous recovery.



Fig. 299.—No. 688. Inhalation ether, automatic. First part of tracing, no anesthesia. Surgical anesthesia in about two minutes. Note on tracing good result of careful induction and use of air with ether.



Fig. 300.—No. 319 b. Inhalation ether, automatic. Note in middle third of tracing the effect of uneven administration of anesthetic. Upper tracing, cardiac; lower, respiratory. Spontaneous recovery.



Fig. 301.—No. 676. Intravenous chloroform, 1.5 per cent. First part of tracing, local anesthesia. Note effect on cardiac action during induction of anesthesia. Spontaneous return to normal.

Finally, praiseworthy and seemingly progressive as are the various endeavors which are being made in the application of new general anesthetics and methods, nevertheless it appears that one of the most essential steps, if not, indeed, the most essential step, toward placing the question of anesthesia on an efficient basis is the training and encouragement of the skilled anesthetist.

## DATA FROM THE MAYO CLINIC

From the year 1900 to the beginning of the present year the respective numbers of general anesthetics administered were as follows: Ether, 49,057; chloroform, 1300; nitrous oxid (usually nitrous oxid ether sequence), 1000; and ether-chloroform sequence, 796. The nitrous oxid administrations were made during the years from 1900 to 1904, inclusive. Since 1907 chloroform alone has been employed in one case. The mode of administering ether is the so-termed "drop" method. Besides the before mentioned, several of the local anesthetics were employed.



Fig. 302.—No. 687. Intravenous chloroform, 2.5 per cent. First part of tracing, local anesthesia. Total solution, 475 c.c.; chloroform, 11.87 c.c., in eleven minutes. Note cardiac and respiratory failure. Efforts at resuscitation futile.



Fig. 303.—No. 621. Intravenous chloroform, 2.5 per cent. Note induction and failure in first and middle third. Cardiac action and respirations ceased almost simultaneously. Efforts at resuscitation effectual.



Fig. 304.—No. 217. Inhalation chloroform, automatic. Note primary cardiac and respiratory failure and the effect of prompt artificial respiration by tracheal insufflation. Duration of anesthesia, one hour and four minutes.

No death ascribable to the anesthetic alone has been noted. None of the present anesthetists has even administered a stimulant hypodermically during operation. Excitement in the initial stages of anesthesia has been very rarely observed. Postanesthetic effects, such as nausea and vomiting, have been, as a rule, inconsiderable.

## PRELIMINARY ADMINISTRATION OF DRUGS

In cases of exophthalmic goiter in which operation was performed without general anesthesia, scopolamin,  $\frac{1}{200}$  grain, and

morphin,  $\frac{1}{8}$  grain, is used. If a general anesthetic is to be administered, atropin,  $\frac{1}{150}$  grain, is also employed. In operations for ordinary goiter morphin,  $\frac{1}{8}$  grain, and atropin,  $\frac{1}{150}$  grain, are used. In operations on the stomach and rectum morphin,  $\frac{1}{8}$  grain, is used. If a patient has had bronchitis or a cold, morphin,  $\frac{1}{8}$  grain, and atropin,  $\frac{1}{150}$  grain, is employed. Scopolamin and morphin are administered to quiet nervousness, but apparently as a result

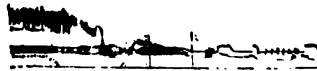


Fig. 305.—No. 687. Inhalation chloroform, automatic. Note early cardiac failure and futile efforts at resuscitation.

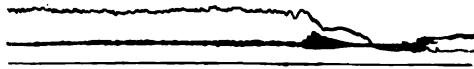


Fig. 306.—No. 634. Intravenous ether, 5 per cent. First and second thirds of tracing, no anesthesia. Last third shows effects of air entering tube during induction of anesthesia—about 100 c.c. air. No recovery, despite efforts at resuscitation. This indicates the danger of a defective apparatus.

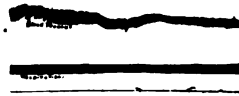


Fig. 307.—No. 683 b. Intravenous ether, 5 per cent. Surgical anesthesia. Tracing shows absence of evil effects when tube to vein is completely severed while solution is flowing.



Fig. 308.—No. 665. Local anesthesia. Air-embolism syringe, 60 c.c. air, in fifteen seconds. Spontaneous recovery.

increased excitement has been occasionally observed. It is considered probable that following the use of these drugs a smaller amount of the general anesthetic is necessary. In operations on the stomach the preliminary dose of morphin makes it feasible to decrease the amount of general anesthetic during the work in the abdominal cavity. Atropin causes and maintains a dry condition of the upper portion of the respiratory tract and is regarded by the anesthetists as very effective when indicated. Generally speaking,

however, ether alone is used, the aforesaid drugs being employed only in exceptional cases under special indications.

The object aimed at is to guard against impurities in the anesthetic, to induce anesthesia with the least possible mental and physical disturbance of the patient, and to employ the smallest amount of anesthetic consonant with an even surgical anesthesia.

As may be gleaned from an analysis of the records, ether by the drop method, in the hands of skilled anesthetists, indicates the position of the Mayo Clinic on the question of general anesthesia. The present tendency of the clinic is toward amplifying the employment of local anesthetics.

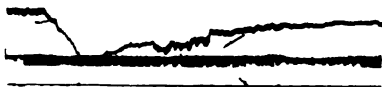


Fig. 309.—No. 408. Intravenous ether, 5 per cent. Note effect of air-embolism—syringe, 100 c.c., air in fractional injections in first part of tracing. Spontaneous recovery. Light anesthesia.



Fig. 310.—No. 649. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note induction of anesthesia in first third of tracing, effect of air-embolism, about 60 c.c. slowly, in middle third. Spontaneous recovery, light anesthesia, but sudden cardiac and respiratory failure after a small dose of ether. Unsuccessful efforts at resuscitation.



Fig. 311.—No. 673 b. Intravenous ether. Air-embolism—50 c.c. air in fractional doses, few seconds apart. Compare effect on heart, upper line, with respirations. Spontaneous recovery.

### EXPERIMENTAL OBSERVATIONS

During the past three months I have been pursuing experimental investigations on the subject of general anesthesia. The work thus far done is admittedly academic, but designedly presented at this stage not so much for discussion of the indefinite results obtained as for criticism of the procedure as a method of studying and teaching the subject. The object in view is to continue the work at length, investigating the various recognized anesthetics and methods, whatever new may be advanced, studying not only immediate but also remote effects on the organism, and

prolonging the work in series sufficiently extensive for deductions of practical value.

One hundred and fifty-three experiments have thus far been undertaken on 145 dogs. The anesthetics employed are ether, chloroform, paraldehyd, combined paraldehyd and ether, urethane, and nitrous-oxid-oxygen-ether.

The methods of administration used are the intravenous, automatic inhalation, insufflation, and rectal. Kymographic records of cardiac action and respirations have been constantly made.

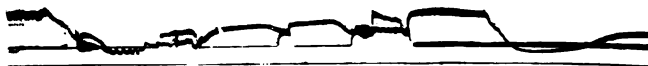


Fig. 312.—No. 646. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note early respiratory and later cardiac failure. Efforts at resuscitation successful. Air-embolism, about 70 c.c., slowly injected. Shown in last third of tracing. Spontaneous recovery.

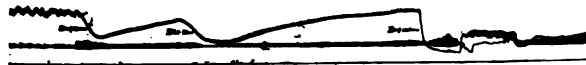


Fig. 313.—No. 637. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. Note cardiac action and respirations during induction of anesthesia. Final third of tracing is a picture resulting from an injection of about 50 c.c. air into femoral vein, tracheal insufflation of air and abdominal pressure. Recovery during light anesthesia.

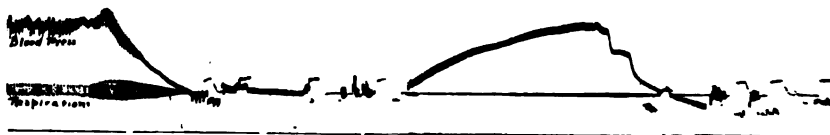


Fig. 314.—No. 678. Intravenous ether, 5 per cent. First part of tracing, local anesthesia. In first third of record note very early cardiac and respiratory failure. In middle third effectual efforts at resuscitation. In last third fatal effect of air-embolism—about 80 c.c. air within twenty seconds. Help ineffective.

Owing to the brevity of the time and the extent of the work, the investigation of some of the anesthetics and methods has been too limited for presentation.

Ether has been administered intravenously 85 times, chloroform 19, paraldehyd 2, and combined paraldehyd and ether 3; by the pulmonary route, ether 27 times and chloroform 8. Besides these experiments, a series of histologic examinations has been begun for the purpose of studying the effects of the various anesthetics on the tissues of the body. An endeavor will be made to



make this work as complete as possible, and sufficiently extensive for data of value. Although some excellent observations have been reported on this phase of the subject, still it seems that in general attention has been mainly focused on the immediate deleterious effects of anesthetics, somewhat to the neglect of their remote effects on the organism.

In the present limited series the procedure has been to study immediate effects during the induction of anesthesia, the results of overdosing, uneven administration, anesthetics with probable impurities, and the efficacy of various methods for resuscitation ap



Fig. 315.—No. 674. Intravenous ether, 5 per cent. First part of tracing, no anesthetic. Note primary anesthesia with early respiratory failure and its relation to cardiac failure. Artificial respirations and heart massage; recovery and again failure on adding small amount of ether. Recovery with help. Air-embolism—60 c.c.—syringe. Sudden and fatal cardiac failure. Slight spontaneous efforts at respiration toward end.



Fig. 316.—No. 680. Inhalation ether, automatic. Light anesthesia. Total amount of air injected into femoral vein, about 300 c.c. First drop is effect of 100 c.c. air in twenty seconds, second and third drops, 100 c.c. air in fifteen seconds each. Note that respirations are little affected. Recovery, but animal died two days later. Air in heart and quite generally in veins.

plied early and late in cardiac and respiratory failure, such as insufflation, abdominal pressure, heart massage, and stimulating drugs injected directly into the circulation. With local anesthesia it has been practicable to obtain normal tracings of cardiac action and respiration for comparison with the various phases of the tracings which followed.

The intravenous method has been employed 109 times. In normal saline solutions the following strengths of anesthetics have been used: ether, 5 and 3 per cent.; chloroform, 2.5 and 1.5 per cent.; paraldehyd, 2 per cent.; ether, 5 per cent.; and paraldehyd, 1 per cent. Hedonal and other anesthetics will be added to the

list in the further progress of the work, and Ringer's solution will replace the saline solution which has been used.

#### AIR EMBOLISM

The question of air embolism has been studied in association with the experiments on intravenous anesthesia. This has consisted of the injection into the femoral vein of large amounts of air, from about 50 to 100 c.c. at once, and large amounts fractionally. Observations on the effects of air embolism have been made with local, light and deep general anesthesia.

As previously intimated, the results of experimentation will not be discussed at this time. A clearer idea of the plan of the work is better seen depicted on the limited number of the accompanying kymographic records.

## ETHER ANESTHESIA\*

FLORENCE HENDERSON (R. N.)

Ether has been used almost exclusively in the Mayo Clinic for many years, and in spite of the fact that in many other places it is employed less frequently than formerly, the surgeons here have not become convinced that it is not the anesthetic to be preferred. Formerly it was thought necessary to use chloroform in certain cases, but the indications for its use have disappeared and for the past five or six years it has not been employed.

It may be noted that in articles in which comparisons are made between nitrous oxid and ether conclusions are drawn from results obtained by the expert with the former anesthetic and those of the inexperienced anesthetist with ether.

The fact that ether is so safe has led to its abuse. The trained anesthetist is not demanded, the administration often being in the hands of the least experienced physician on the staff, who while his results are not satisfactory, is allowed to give the anesthetic because the patients survive. For the administration of nitrous oxid, however, a physician with experience is selected. If he would devote the same amount of time to learning how to use ether that he does to learning how to use nitrous oxid, there would not be the difficulties from its use which are so often described.

In an editorial in the London Lancet for February 1, 1913, the statement was made that: "In this country (England), where the possibilities of nitrous oxid and oxygen were originally investigated by Sir Frederick Hewitt many years ago, the general sentiment is that the method has serious limitations, especially imperfect relaxation, difficult and complicated technic, and expense."

\* Read before the South. Minn. Med. Assoc., December 2, 1913. Reprinted from the St. Paul Medical Journal, February, 1914, pp. 74-82.

If nitrous oxid were given as carelessly as ether very often is, there would be so many fatalities that its use would be prohibited.

In selecting an anesthetic we must consider—(1) Its safety; (2) its anesthetic properties; (3) the after-results upon the patient; and (4) the convenience of the surgeon.

Statistics show that ether as an anesthetic is superior to all others in safety and range of application. If given properly, very few patients find it disagreeable, and the after-results compare favorably with those of other anesthetics. The surgeon can work with more ease and rapidity because relaxation can be secured. He is not handicapped in making thorough examinations by troublesome rigidity. In some cases the surgeon is to be blamed for insisting upon a too profound anesthesia, since to secure it the narcosis must be carried to a dangerous point. If, in very serious cases, he would exercise the same care in manipulation that is observed when nitrous oxid is used, and be content with as light anesthesia, he would probably find that his patients would recover as rapidly and without the shock and unpleasant after-effects which are quoted as contraindications to the use of ether.

In giving ether the difficulties encountered by many anesthetists are more often caused by doing too much rather than too little. If the patient is carefully watched and not disturbed while doing well, the anesthetist will seldom meet with alarming conditions. Gaining the confidence of the patient aids materially in securing a rapid and comfortable anesthesia. Patients who can be interested in something foreign to the work in hand will usually "go under" the anesthetic more rapidly. After gaining the confidence of the patient, surgical anesthesia ordinarily may be produced by the drop-method with ether in from three to five minutes.

This being accomplished, if the air-passages are kept free; if the jaw is kept forward and up; if sufficient air is admitted with the ether to keep the patient's color good; if the ether is continued by slow and regular drops; and if the patient is watched constantly, all is done that is necessary in the ordinary case. The management of the jaw has much to do with the success or failure of the anesthetic. If the jaw is kept forward and up so that the tongue

cannot drop back, there will be no necessity for the use of the mouth-gag or tongue-forceps. The infrequency with which difficulties are encountered when the above rules are observed is remarkable. To avoid trouble is much easier than to overcome it when once encountered. With these precautions there will be less vomiting and the patient need not be so deeply anesthetized to prevent vomiting. In some cases an oral air-passage is maintained as the best means of securing free breathing.

It is desirable that ether be given in a well-ventilated, quiet room, where there is nothing to distract the patient's attention from the anesthetist. Quietness suggests sleep. In the Mayo Clinic the anesthetic is always administered to the patient in the operating-room. Any prejudice which the patient may have against being anesthetized in the operating-room is easily overcome when he realizes that it is for his benefit. Moreover, the surgeon is at hand, and, while the patient may not have confidence in the anesthetist, he has all confidence in the surgeon. The anesthetic can be given while the field of operation is being prepared, thus saving time and shortening the length of the narcosis. When the anesthetic is given in an outside room, some one usually has to wait, and more often it is the patient than the surgeon. The degree of anesthesia must be deep, or the patient will vomit while being moved from one room to another. Some observers contend that giving the anesthetic in the operating-room wastes too much time. We find that the usual time between the final sutures in one operation and the making of the incision in the following operation is but ten minutes, five of which are consumed in applying the dressings, removing the patient from the room, and putting the next patient upon the table. The remainder of the time is spent in the preparation of the patient, who is being anesthetized while this is in progress. The surgeons believe that the sacrifice of this amount of time is well worth while when the benefit derived by the patient is considered.

The patients are placed upon the table in the position in which they are to lie during the operation, and the anesthetic started at the same time as is the preparation. The head is made comfort-

able, and the mouth examined to see that it contains no artificial teeth, foreign bodies, etc. The hands are fastened at the sides to prevent the arms from falling to the side of the table, and thereby causing pressure on the musculospiral nerve. The lower limbs are wrapped in a blanket and a brace slipped over them just below the knees. The patient's eyes are covered with a pad of wet cotton, and, if his position is such that the cotton does not remain in place readily, a piece of gutta-percha tissue is used in addition under the cotton.

A modified Esmarch inhaler, which is covered with two layers of stockinet, is used. It is sterilized, and a fresh cover applied after each case. For convenience in handling, ether is dropped from a four-ounce can or bottle which has a cork with notches on opposite sides, through one of which a small wick of cotton is passed into the can. With the mask held about an inch from the face the ether is dropped upon it, slowly at first, and the patient is asked to breathe naturally through the nose. Then the mask is gradually lowered, and the rapidity of the dropping increased, care being taken not to give the ether fast enough to cause a sensation of smothering or suffocation. As the ether begins to affect the patient, as evidenced by the face becoming flushed, a width of gauze about a yard long, which is folded to four thicknesses, is wrapped partly around the mask, and finally completely around it, with the exception of a place for air. The ether is then dropped more rapidly. As soon as the jaw relaxes the head is turned to one side, because the patient usually breathes more easily with the head in this position. If ether is given too rapidly, the patient manifests excitement, and the mask should then be removed and more air allowed. An occasional breath of air without ether hastens the narcosis and does away with any feeling of suffocation. A properly administered anesthetic should have no stage of excitement if the patient is given only the amount of ether he can take comfortably.

The discomfort experienced by the patient while "going under" may be avoided by the anesthetist, and a smooth, uniform nar-

cosis maintained, which will keep the patient asleep and relaxed throughout the operation.

Surgical anesthesia is recognized by the deep, regular breathing and by relaxation of the muscles. It is not often that it is necessary for the surgeon to inquire, "Is the patient ready?"

The patient should never be crossed, but always made to feel that he is having his own way in taking the anesthetic. The patient is assisted materially if the anesthetist explains the progress of the narcosis and prepares him for the stages as they appear. Suggestion plays an important part in the induction of anesthesia, and the fact that the administrator is talking to the patient assures him that the attention of the anesthetist is upon him. If a patient fears anything, usually it is that the operation will begin before he is asleep. The assurance of the anesthetist, when the patient is in the subconscious state, that he is all right and that nothing will be done until he is unconscious, aids markedly. The mind is very susceptible to suggestion in this state, and the suggestion that everything is as it should be is usually accepted. It is true that patients must be treated differently according to the temperament of each individual, but the majority of them will respond to encouragement and the reassurance that they are doing well. The frightened, ignorant patient, who is apprehensive that something might be done of which he is unaware, is harder to deal with than the intelligent, reasonable one. The robust, florid patient, who is not ill at the time of the operation, is much more likely to be frightened than the very sick patient, who has suffered greatly and is anxious to obtain relief.

The depth of anesthesia depends upon the kind of operation and its stage. The patient should never be kept more deeply under the anesthetic than is consistent with the work of the surgeon. Head and neck operations can usually be carried along with a light degree only. Patients with peritonitis require more anesthetic than those with chronic or subacute abdominal lesions. Abdominal operations, especially those in the pelvis and upper abdomen, require deep anesthesia to produce relaxation, which will enable the surgeon to do satisfactory work. Gastric and intes-

tinal cases may be conducted under light anesthesia after the examinations have been made and the work upon the viscera begun. There is no pain connected with such manipulation, but when the parietal peritoneum is to be closed, the patient must have more anesthetic. As soon as the peritoneum is closed, in most cases, the anesthetic can be withdrawn, and the patient is usually awake by the time he reaches his room, and often before he leaves the operating-room.

In serious cases in which it is desirable to use local anesthesia, as in the cases of toxic goiter that are associated with terminal degenerations in vital organs or in cases of severe exophthalmic goiter, we have found the administration of a small amount of ether to be advantageous in allaying nervousness. A hypodermic of  $\frac{1}{200}$  grain scopolamin and  $\frac{1}{6}$  grain morphin is given from one to two hours before operation. The line of incision is injected with 0.5 per cent. solution of novocain, a considerable quantity being used. The incision may then be made, and the flaps dissected without ether. While the muscles are being separated, a little ether may be given, that by the time the surgeon is ready to dissect the gland from the trachea, causing pain and giving rise to a feeling of suffocation, the patient is under primary anesthesia. In most cases this condition will continue, with the administration of a few more drops of ether, until the deep vessels are ligated. While the incision is being closed there is no pain, since the skin has been infiltrated. In this way patients may be carried very comfortably through an operation with from but one-half to one ounce of ether. This method also is useful in prostatectomy cases, which are usually poor risks. Rectal cases require full anesthesia, while extraperitoneal operations, those upon the extremities, breast, etc., may be conducted under light anesthesia.

Primary anesthesia may be used in minor operations. If the surgeon begins the operation as soon as the patient is asleep and the anesthetic is withdrawn at that time, the patient is awake by the time the operation is completed and the dressings applied. Experience in the Mayo Clinic does not show that shock is produced by light ether anesthesia, as is stated by many writers.



There can be no rule as to how much ether to administer in any given case, but each patient should have the smallest amount practicable. The dose should be medicinal and not toxic. It should be given with regard to its physiologic action, as should any other drug. For operations the duration of which averages about forty minutes, patients usually require between three and four ounces of ether to produce anesthesia and to carry them through the operation.

Postoperative vomiting is present in a small percentage of cases, but it is seldom persistent, like that following chloroform. When ether is given in toxic doses and the blood becomes saturated with it, the stomach is called upon to aid elimination, and nausea and vomiting are the natural consequences. Transient vomiting is not always a disadvantage, since it clears not only the stomach, but also the lungs. Single emesis, which frequently takes place just before the return of consciousness, is oftener than not an advantage.

Preliminary medication is to be used only in selected cases, and not as a routine. Patients with simple goiters are given  $\frac{1}{6}$  grain morphin and  $\frac{1}{150}$  grain atropin one-half hour before operation. The atropin prevents the formation of mucus which comes from manipulation of the trachea. In gastric and rectal operations the patients are given  $\frac{1}{6}$  grain morphin before operation. Patients with pulmonary complications receive  $\frac{1}{6}$  grain morphin and  $\frac{1}{150}$  grain atropin.

Pulmonary complications which can be attributed to the anesthetic are rare. The few pneumonias which are seen usually develop from several days to a week after operation, and occur mostly in upper abdominal cases. On account of the location of the incision near the diaphragm these patients do not take deep inspirations after operation. They thus fill only a part of their lungs. This fact makes it possible for septic pneumonias to develop from embolic infarctions.

To become skilled in the administration of ether the anesthetist must devote all her time to it, and only after much experience can she expect to do creditable work and secure satisfactory

results. The mental attitude and feelings of the anesthetist are reflected upon the patient. If the administrator is nervous or loses confidence in her ability to secure a rapid narcosis, it invariably affects the patient. The anesthetist should pay enough attention to the different stages of the operation to know when to increase the anesthetic and when to decrease it or to withdraw it entirely. The surgeon has a right to expect the anesthetist to attend to this part of the work and to feel that he need not divide his attention between the narcosis and the operation. It should seldom be necessary for him to inquire as to the condition of the patient, and, with ether properly administered, the occasions when alarming symptoms arise are very rare. The anesthetist should not, however, become interested in the details of the operation.

Before the discovery of anesthetics an operation was a formidable procedure, and, as far as narcotics could be used to relieve pain, they were employed freely preliminary to the operation. Then came the discovery of chloroform and ether, the former recognized as a very dangerous drug, always to be handled with great care, and its administration intrusted to a competent man. The safety of ether was its own undoing. It did not kill, and so its administration was intrusted to the most incompetent person. Then came nitrous oxid, an inefficient surgical anesthetic at best, and finally local anesthesia, which, next to ether, has the widest field of usefulness.

Today we are going through a curious phase in the use of anesthetics, namely, a return to narcotics, inefficient nitrous oxid, and local anesthesia, a combination which has the bad qualities of all three, and in which the local anesthesia does most of the work.

There is no doubt that local anesthesia can be used in an increasingly large number of cases. Ether given by the drop method by a skilled anesthetist and local anesthesia certainly fulfil the requirements more satisfactorily than any other anesthetic or combination of anesthetics known at the present time.

## THE USE OF NOVOCAIN AS A LOCAL ANESTHETIC\*

DONALD C. BALFOUR

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The field of application of local anesthesia in present-day surgery is undoubtedly becoming broader. Notwithstanding the fact that general anesthesia has reached its highest development in this country, abolishing pain by analgesics employed locally is more popular with American surgeons than was the case a few years ago, chiefly because with modern methods safe and efficient anesthesia can be obtained. The improved technic may be attributed to the investigations of various observers, notably, Scheiffe, Kocher, Bier, Bastianelli abroad, and Crile, Mitchell, Cushing, and others in this country.

The remarkable success of local anesthesia on the continent, its prevalence and variety of application, is rather a commentary on the standard of general anesthesia existing there. It is probably true that local anesthesia will never attain in this country the position it holds on the continent at the present time. This can be attributed to two reasons: (1) The American surgeon is well satisfied with a general anesthesia under ether administered by a skilled anesthetist; (2) he will not, as a rule, give the patience nor the time that is so necessary in order to derive the ideal results which should obtain from the use of local analgesics. Nevertheless, one observes that its use is increasing in popularity in this country among men who are doing progressive surgery. This may in part be due to the fact that superior derivatives of and substitutes for cocain have been placed on the market. The more

\* Read before the Southern Minn. Med. Soc., Owatonna, December 2, 1913. Reprinted from St. Paul Med. Jour., February, 1914, pp. 83-90.

familiar of these are eucain, stovain, tropacocain, novocain, urea, and quinin hydrochlorid.

It is my purpose in this paper to give briefly the results obtained in the Mayo Clinic with the use of novocain during the past year. This drug has been so consistently satisfactory that other preparations, of which such favorable results have been reported by other observers, have been little used in this clinic.

A note as to the properties of novocain might not be out of place. The powder is rapidly soluble, and the solution can be boiled without destroying its effectiveness. In poisonous doses spasms occur. The safe maximum dose has been stated to be about 7 grains. The duration of the anesthesia, when used without an adjuvant, is fifteen minutes (Hertzler), but its action is more prolonged when adrenalin is added.

The advantages obtained in the use of this preparation are definite and important, the most satisfactory of which is that the solution (0.5 to 1 per cent.) can be used in almost unlimited quantities without fear of ill effects. This permits a wide infiltration of the operative field, with liberal blocking off of the sensory nerve supply, which is not permissible with cocain unless the latter be used in such large dilutions that the anesthesia is dependent to a considerable extent on the edema produced, and not the cocain itself. The fact that the novocain solution can be boiled without affecting its analgesic property is of decided advantage. We have not had sufficient evidence to show that healing of wounds is definitely retarded by the infiltration of the tissues by the solution. In the experience of several surgeons the use of double chlorid of quinin and urea has been followed by serious sloughing.

Reference to the operations performed in the Mayo Clinic during the past year under regional anesthesia with novocain gives a fair representation of the conditions in which its use is indicated, since in these cases it has been used in preference to a general ether anesthesia which is considered safe and results in practically no serious after-effects.

The largest group in the series is made up of cases in which the operation entails no exploration, is expected to be simple, and not

prolonged. In this group we have ligation of arteries, particularly those of the thyroid, removal of small tumors of the breast, superficial cysts, lipomas, circumcision, paracentesis, external hemorrhoids, drainage of abscesses, excision of isolated glands and specimens of tissue for diagnosis, tonsillectomy in the adult, and various operations on the nose and throat.

Another group is composed of cases in which a general inhalation anesthesia is preferable, but might, for some reason, be deleterious to the patient. In this class we have patients with recent acute conditions of the lung, alcoholism, nephritis, myocarditis, etc., or any complication which renders ether not necessarily prohibitive, but rather inadvisable. Under these circumstances hernia, hydrocele, varicocele, tuberculous epididymitis, varicose veins, and similar conditions are very satisfactorily operated on under local anesthesia. Operations on the thyroid are often necessary with an unstable nervous system and marked degenerative changes in the heart and kidneys. In these cases, also, a local anesthesia is preferable. However, no rule can be absolute, and each patient must be considered individually. For example, those patients in whom continued thyroid intoxication, due to a degenerating adenoma, has produced marked terminal changes in the vital organs, with mental irritability and physical restlessness as predominant features, and in whom a preliminary ligation would afford no improvement, can be carried much more safely through the operation under a light ether anesthesia than by attempting to perform it with novocain. One here observes the important element of personal equation; on the one hand, individuals under an apparently unreasonable excitement; on the other, in the apathetic state which is so desirable in obtaining a satisfactory local anesthesia.

Of great importance, too, is the relationship between patient and surgeon, especially the degree of confidence the patient entertains for the surgeon, and the support given by the surgeon in praising the patient's courage, even though it may not be much in evidence. An explanation of what is to be done and what is to be expected is helpful with most patients.

The advantages of a combined anesthesia are particularly applicable in surgery of the thyroid when the condition of the patient indicates that the smaller the quantity of ether used, the better. It is satisfactory in these cases to make the skin incision, divide between the muscles in the midline, if necessary cutting the sternohyoid and sternothyroid under local anesthesia. An excellent exposure of the gland can thus be obtained painlessly. After beginning the actual extirpation of the gland, it is well to allow the patients to decide whether the pain is unbearable; if so, a few inhalations of ether will quiet them and enable the operator to remove the portion of thyroid which is necessary.

Another group, which is relatively small, is composed of those patients who request that a local anesthesia be used. Few individuals voluntarily choose to have any operation, however slight, performed "under cocain." In fact, it is rather the rule to have patients object to the suggestion of a local anesthetization, the most frequent reason being that they do not want to know "what is going on."

Formidable operations may be accomplished in the group of cases in which an inhalation anesthetic is practically prohibitive, and one is forced to use a local anesthetic. Such operations include extensive dissections of the neck, amputation of limbs, prostatectomies (spinal anesthesia is best for the latter), and certain intra-abdominal operations.

During the past year several abdominal operations have been performed under novocain alone in our clinic, among these being appendectomies, gastrojejunostomies, gastrostomies, cholecystectomies, and the removal of ovarian cysts. Although the possibilities in this class of cases are decidedly limited, yet more and more extensive operations are being performed, confining them to well-defined conditions that can be corrected by a minimum amount of manipulation. For example, an appendix can be satisfactorily removed through a split-muscle incision if it is not markedly adherent. On the other hand, should old firm adhesions be present and considerable traction necessary to free the appendix, severe pain will be produced which cannot be controlled by any method

of injecting an anesthetic. This fact, therefore, renders intra-abdominal operations unsatisfactory under local anesthesia, chiefly because a thorough exploration is impossible and restricted to the few cases in which the procedure is obvious.

Operating under local anesthesia has no advantages and may have distinct disadvantages to the operator. The so-called "co-operation of the patient" is a doubtful factor, as it is sometimes decidedly not in evidence. The operation is rendered more difficult because of the surgeon's desire to spare the patient as much pain as possible. He hampers himself by insufficient exposure and attempts to accomplish what is necessary by as little manipulation as possible. However, by the skilful use of the anesthesia and by the careful injection of the tissues layer by layer the amount of pain to which the patient is subjected becomes less and less. The dissection under such conditions is of necessity cutting with knife or scissors; gauze dissection is practically prohibited.

The advantages in the employment of novocain are almost entirely on the side of the patient, although unfortunately freedom from pain in the infiltrated area is not insured for any length of time following operation, as is claimed for other substances. Interference in the healing of wounds by the devitalization of the tissues has not been observed in our cases to any appreciable degree. Postoperative nausea, vomiting, and thirst are much less frequent in occurrence than after ether anesthesia, except in cases of severe hyperthyroidism, when the gastro-intestinal disturbance is a part of the disease.

The methods we have found satisfactory in preparing and using novocain are as follows: A sufficient quantity of a 0.5 or 1 per cent. solution is made by dissolving the novocain in sterile water. This solution is boiled for two or three minutes, and enough adrenalin is added to the solution to make a strength of 1:1000. We do not employ thymol nor any other preservative agent to render the solution stable. A fresh mixture should be made for each operation.

The method of injection varies according to the condition and situation. In acute abscesses, superficial growths, and lipomas it

is best to encircle the field of operation at the base with a substantial infiltration, then wait five or ten minutes before proceeding with the operation. In the majority of instances this gives absolute anesthesia. For ligation of the superior thyroid vessels injection along the line of incision of about 15 c.c. of the solution, 10 c.c. posterior to the outer limit of the proposed incision to block off the superficial cervical nerves in that region, and another 5 or 10 c.c. injected deeply around the superior pole of the gland, usually gives a perfect anesthesia despite the fact that these patients are extremely irritable mentally. For thyroidectomies the same general plan is followed, except that the deep injections around the gland, when it is exposed, are not employed. The time expended in any effort to allay the pain of handling the gland and traction is not advisable. In herniotomy, after the inguinal canal is opened, the cord and sac should be infiltrated as high as possible. The separation of the sac can then be accomplished within a few minutes with very little pain, and a high removal can be done with surprising ease to the patient. In intra-abdominal work it is simple enough to cut through the abdominal wall to the peritoneum without producing pain, but anesthetizing the latter is difficult and oftentimes inefficient.

In general the production of a local edema, allowing a few minutes for the solution to take effect and incising in the edematous area, has been found safe and satisfactory. In the more extensive type of operation morphin,  $\frac{1}{8}$  grain, either alone or, in the case of the hyperplastic goiters, combined with  $\frac{1}{200}$  grain of scopolamin, has been given. In the majority of cases this constitutes a very important adjuvant to the successful use of local anesthesia of this type.

In conclusion I would emphasize the belief that in novocain we have a safe and efficient means of producing local anesthesia, that the possibility of its application outside the abdominal cavity is almost without limitation, and that it is invaluable to the surgeon who is unable to secure a skilfully administered general anesthetic.



## A NEW MOTOR MEAL AND LAVAGE TUBE\*

FRANK SMITHIES

Stomach-tubes, as ordinarily made, seem to have the following faults: (1) The inferior rubber in their construction, which prevents sterilization by boiling (the only efficient method); (2) small lumina, which frequently render unsatisfactory the aspiration or expression of motor meals or poorly chymified test-breakfasts; (3) improperly placed, too few or too small fenestra at their distal ends; (4) the incorporation into the tubes of "aspirating bulbs" of questionable service, which are difficult to keep clean.

In an effort to remedy some of these defects we have had constructed tubes of the type to be described. They have given greater satisfaction than any other form in the last 1500 cases in the Mayo Clinic in which the test-meal examination was made.

The tube is constructed† of best quality of red rubber. The wall is 2 mm. thick and the lumen has a diameter of 6 mm. The tube is made in two sections, distal and proximal, connected by a thin, but strong, aluminum mid-piece.

(1) The *distal segment* of the tube is 90 cm. long. It has a distal opening of 1 cm. diameter. Beginning 1 cm. from this tip is a lateral fenestrum (Fig. 317) of ellipsoid form, 2 cm.

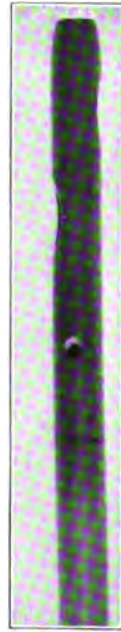


Fig. 317. — Distal end of tube, showing arrangement of fenestra.

\* Reprinted from Jour. Amer. Med. Assoc., February 7, 1914, pp. 453, 454.

† These tubes in Goodyear make.

long and 1 cm. wide. On the opposite lateral surface to this is a second similar lateral fenestrum, which begins 3 cm. from the tip of the tube. The fenestrum is placed at this point not only to permit free siphonage of gastric contents, but also to facilitate the introduction of the tube. Its location, 3 cm. from the tip of the tube, is the average distance in different individuals from the pharyngeal bend of the tongue to the *introitus œsophagi*. When the tip of the



Fig. 318.—Full view of tube, showing segments, markings, and fenestra on distal segment and aluminum midpiece. Segments separated to show this.

tube enters the pharynx with the second lateral fenestrum toward the tongue, the subject's swallowing motions promptly bend the tube at this fenestrum, and the tip glides readily into the esophagus. Using a tube with a distal end of this type, the larynx has not been entered more than a dozen times in our last 5000 cases. Eight centimeters from the tip of the tube are placed three round fenestra, of a diameter of 2 mm. They pierce the tube at the same level. This distal segment of the tube, beginning 10 cm. from its

tip, is marked off by encircling black lines (Fig. 318) every 5 cm. for a distance of 55 cm. from the distal end. These markings permit of fairly accurate location of obstructions in the esophagus. The tube in such instances acts as a hollow sound through which the contents of esophageal sacculations and the like may be readily secured.

(2) The connecting *aluminum midpiece* is 5 cm. long, with a wall 1 mm. thick and a lumen 1 cm. in diameter. It is slightly roughened, and fits snugly into the rubber parts. It is non-rusting.

(3) The *proximal end* of the tube is 60 cm. long. It may be replaced when necessary by an aspiration bulb, which fits onto the metal midpiece.

The *advantages* of the type of tube described appear to be—  
(a) *Durability*: these tubes may be boiled for months and still retain their form; (b) The lumen is large enough to permit free expression or aspiration of retention contents after the administration of a motor test-meal; (c) the distal fenestra so placed as to permit the easy passage of the tube and the rapid siphonage or aspiration of gastric contents. Free lavage is readily carried on, either for the purpose of determining retention (as in hour-glass stomach) or for therapeutic effect; (d) the tube acts as a safe and convenient esophageal sound; (e) the aluminum midpiece replaces easily broken glass connections. It enables one rapidly to convert the straight siphon or lavage tube into one of bulbed type for the purpose of inflating the stomach with air and when expression of gastric contents proves difficult.

## ANTERIOR GASTRO-ENTEROSTOMY\*

### Report of a Case of Diverticula of the Jejunum

DONALD C. BALFOUR

It is generally conceded that when a gastro-enterostomy is indicated, the posterior no-loop operation is safer, gives the best end-results, and that it carries practically no risks of unfortunate mechanical sequelæ. The method has been so consistently satisfactory that it may have been used at times when other methods would have sufficed as well or perhaps better. It is particularly applicable for benign lesions in the region of the pylorus when a resection of the pyloric end of the stomach is not indicated or some type of plastic operation is not possible.

For various reasons an anterior gastro-enterostomy is the operation of choice in certain definite groups of cases, the largest of which is composed of the obstructions at the pylorus due to carcinoma in which a resection of the growth is not feasible. In many of these cases the mechanical obstruction with retention of decomposed food products and the resulting starvation are the important factors. These patients are not only greatly relieved temporarily by drainage of the stomach, but the terminal stages of the malignancy are much less pitiable. It is particularly in this type of case that the anterior method is preferable on account of the speed, safety, and simplicity with which it can be performed. A smaller group is composed of certain benign lesions at or near the pylorus where a posterior gastro-enterostomy would be desirable, but not possible because of the presence of certain mechanical conditions. Extensive adhesions, congenital or inflammatory, malformations, etc., may be sufficient to preclude the advisability of

\* Reprinted from *Annals of Surgery*, June, 1913, pp. 903-905.

attempting the posterior method, and yet permit the anterior operation to be done safely and quickly. The case herewith reported is illustrative of such a possibility:

CASE A70173.—J. Mc., male, aged sixty-two years. Examination July 5, 1912. No family history of importance and no previous definite illness. Personal history, extending over some twenty years of gastric distress, which suggested a lesion of the duodenum. The symptoms were somewhat irregular, the chief complaint being a dull epigastric pain coming on about an hour



Fig. 319.—Upper jejunum, showing the three diverticula.

after meals and continuing until the next meal, when the food relieved the pain. There had been no vomiting, no evidence of bleeding, no jaundice and no evidence of acute trouble, no definite history of hyperacidity or hypersecretion. The physical findings were not indicative, and the analysis of the stomach-contents showed a total acidity of 77, free HCl 70, and combined HCl 8. The long-standing trouble and a loss of weight during the past few months warranted an exploration, and the patient was referred to the hospital.

*Operation* (July 12, 1912).—A right rectus incision was made to expose the pyloric end of the stomach and duodenum. A large, thick calloused ulcer was found involving the pylorus and extending  $2\frac{1}{2}$  or 3 inches down the duodenum. The ulcer involved the greatest part of the anterior surface of the duodenum and the peritoneum showed evidence of recent inflammation. The stom-

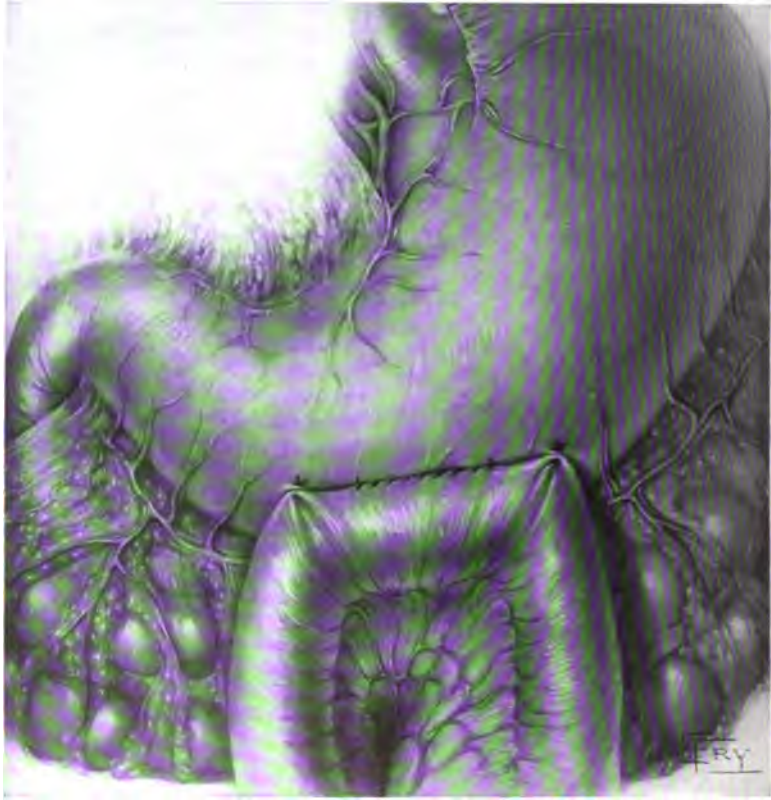


Fig. 320.—Anterior gastro-enterostomy completed, showing the single mattress suture uniting intestine to stomach one inch either side suture line.

ach was negative from the anterior view, the gall-bladder was negative, the appendix showed well-marked evidences of disease and was removed.

The lesion and its situation were typical of the group in which such satisfactory results are obtained by a posterior gastro-enterostomy, and this operation was decided on. On lifting the

transverse colon extensive and apparently long-standing adhesions were found binding the mesocolon and mesentery of the jejunum for several inches along the first part of the jejunum. An examination of the upper jejunum showed the presence of four well-marked diverticula, all showing the same formation. Three of these diverticula were about 16 inches from the origin of the jejunum and within 1 inch of each other, while the fourth was about 4 inches from the duodenojejunal junction. They varied in size from a hazelnut to an English walnut. All were on the mesenteric border of the jejunum, and, since they could be collapsed and would rapidly distend when pressure was removed, were definitely connected with the intestine. They evidently were not causing symptoms and were left undisturbed. Examination of the remaining part of the small bowel showed no other diverticula.

The situation and density of the adhesions to the mesocolon and mesentery of the jejunum, the amount of trauma necessary in order satisfactorily to free the jejunum, made the posterior operation a questionable procedure, and the anterior operation was decided on. This decision was reached after eliminating the possibility of excision or performing a plastic closure of the ulcer itself, chiefly because of its size and the amount of induration surrounding it.

The anastomosis was made just beyond the three diverticula. Probably the most important step in this operation is directed toward the prevention of a kinking at the line of union between the stomach and the intestine, which would mean obstruction and vicious circle. This step is accomplished by a simple method, namely, the Hartmann modification of the Kappler technic, introducing a suture of linen between the stomach and jejunum about 1 or  $1\frac{1}{2}$  inches beyond the extremity of the outside suture line on each side after the anastomosis is completed. This gives the jejunum an attachment to the stomach of nearly double the length of the actual gastro-enterostomy opening and sharp angulation of the actual opening between the stomach and jejunum cannot take place. This method of hitching up the jejunum has probably been the means of preventing the unfortunate complications which were so common following the earlier methods of anterior gastro-enterostomy and for which an entero-anastomosis was so frequently made as a part of the operation.

The patient recovered and was dismissed from the clinic in good condition, and a letter received recently states that he has had no further trouble.

## A SINGLE TRANSVERSE INCISION FOR USE IN DOUBLE INGUINAL HERNIOTOMIES\*

E. S. JUDD

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The use of the transverse abdominal incision and the combined longitudinal and transverse incision is gaining in favor in many clinics. The advantage to be gained in exposure by adding a transverse incision at right angles to a longitudinal one has long been recognized, but this method, unfortunately, has certain disadvantages, such as the difficulty of closing in drainage cases and the occasional sloughing of parts of the abdominal wall from infection, which has prevented many surgeons from using it. Nevertheless the incision, when used in certain regions, undoubtedly possesses definite advantages, and it is probable that it will ultimately be used more frequently, rather in selected cases, however, than as a substitute in all cases for the longitudinal incision.

A partial review of the literature bearing on this type of incision shows that Rapin probably first used the transverse incision; he failed, however, to publish an account of his work. Küstner, working independently, also used the incision about the same time and published a description of his technic and a report of his cases in 1896. Each of these surgeons used this incision solely for cosmetic purposes and intended that it extend only through the skin and subcutaneous fat.

In 1900 Pfannenstiel published a communication describing a method (suggested to him by Küstner's paper) of making a transverse incision through the skin and aponeurosis and a longitudinal one through the muscles. His object differed from that

\* Reprinted from *The Old Dominion Journal of Medicine and Surgery*, April, 1913, vol. xvi, pp. 153-156.



of Küstner and Rapin, and was an effort to prevent postoperative ventral hernia.

Shortly afterward Naudet, an assistant of Hartman, reported cases operated on by the latter, in which the transverse incision had been used.

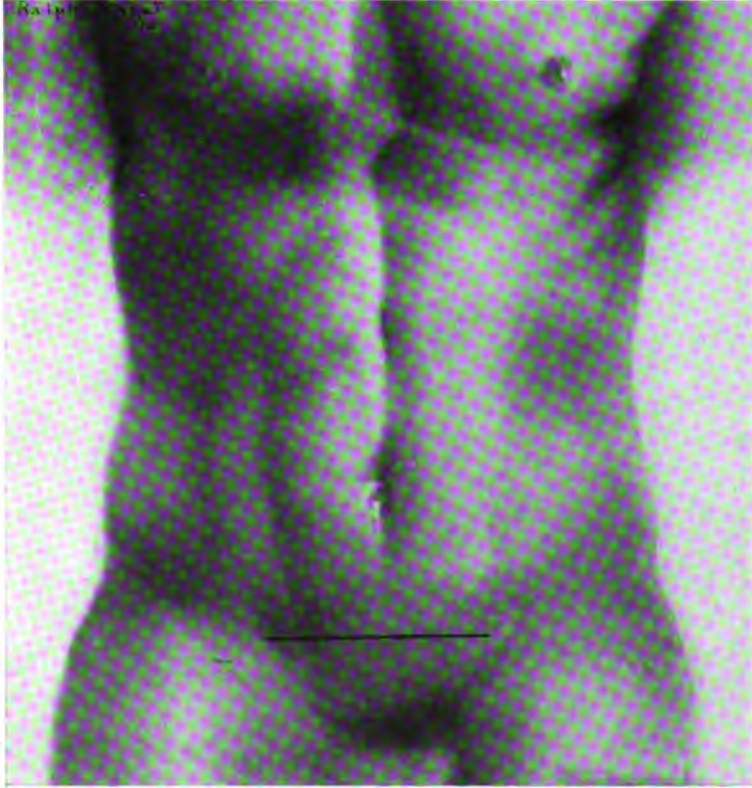


Fig. 321.—Shows incision extending from region of one inguinal canal to the other, from points half-way between the external and internal rings.

In this country, Stimson presented patients operated on by this method and called attention to the advantages gained by its use. Since then other articles have appeared, but most of these have been mere arguments for or against the use of the

method, and few, if any, changes have been made in the technic as originally described by Pfannenstiel.

It has been suggested more recently, especially by Farr, that, when necessary, the recti muscles may also be cut transversely, thus obtaining much better exposure. Some advocates of this method claim that the scar which results after these muscles have healed serves to add another transverse line to the body of the

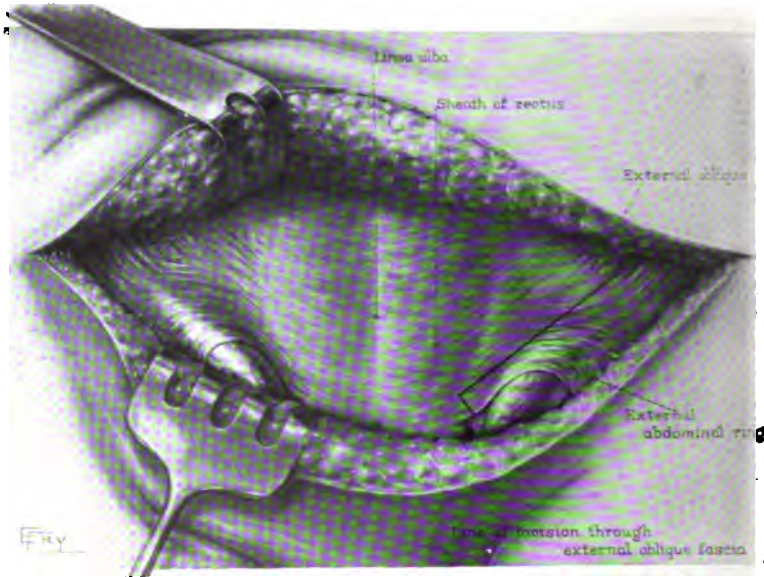


Fig. 322.—Skin and superficial tissue reflected, exposing the fascia of the external oblique and showing external rings and cords. The incision through the external oblique fascia is made one-half inch to the inner side of the inguinal canal in order to make a flap for overlapping.

muscle, and that this line increases instead of diminishes the strength of the muscle.

When first described, the transverse incision was suggested for use only in pelvic work, but it was soon employed as a method of opening the upper abdomen for work on the stomach and gall-bladder.

My experience with the incision in this region has been limited. However, I have found it a very useful one when used in certain

conditions, and am presenting this paper to call attention to some of the advantages which it possesses when used, instead of two oblique incisions, in cases of double inguinal hernias.

In such cases a transverse incision, from 8 to 12 cm. in length, or longer in fleshy patients, is made from a point situated midway between the internal and external abdominal rings of one side to a similar point on the opposite side, thus connecting the two inguinal

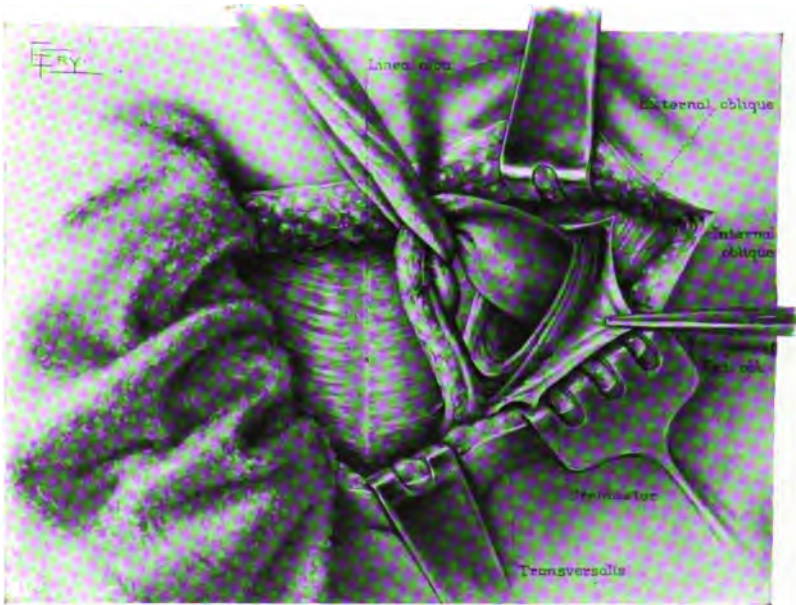


Fig. 323.—Fascia of external oblique has been reflected; cord and sac are lifted up preparatory to dissecting the sac from the cord.

canals. The incision passes directly through the subcutaneous fat and exposes the aponeurosis of the external oblique muscle. The fat around each external ring is dissected away for a short distance and then, by properly retracting the skin and subcutaneous tissues of either end of the incision, the entire inguinal canal of that side will be exposed. The hernia on this side is repaired and then the same retraction is made on the other side for the repair of the second hernia. After the operation on the hernias

has been completed, the superficial tissues are loosely sutured with catgut, and the skin closed either by a subcutaneous catgut suture or a through-and-through horsehair stitch.

With this incision the exposure of either inguinal canal is fully as satisfactory as that obtained when an oblique incision is made directly over the inguinal canal on each side. The entire length of the transverse incision is often not more than that of the oblique

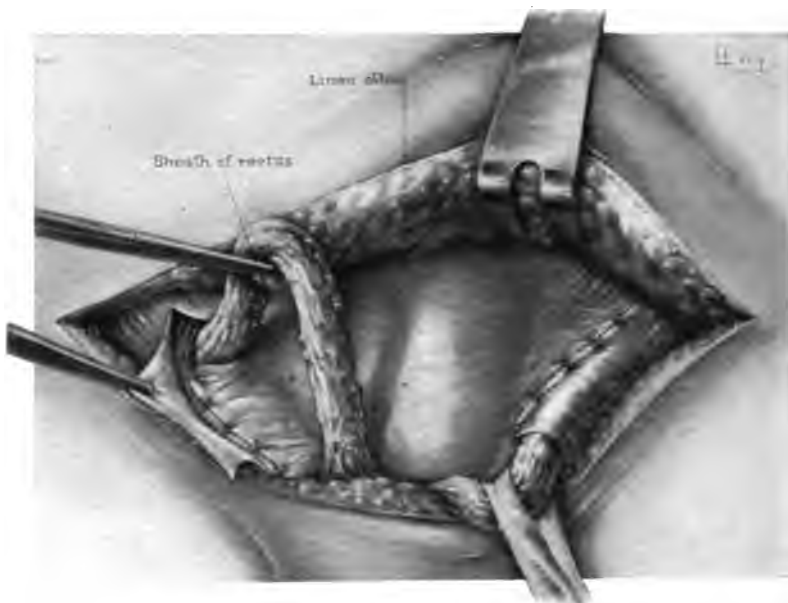


Fig. 324.—Operation complete on one side. Aponeurosis of external oblique, on inner sides of incisions, is included in the stitches through the rectus, conjoining tendon and internal oblique, and is pulled down to Poupart's ligament. Flap of fascia carried over cord and stitched to the surface of fascia, so that cord lies between two layers of external oblique fascia.

incision as it is ordinarily made for the repair of a single inguinal hernia.

The bleeding is very slight, as a rule: only the small branches of the superficial epigastric vessels come into consideration.

One of the principal advantages of this method is seen in those patients who have worn a truss which has compressed and hardened the region or possibly has blistered and broken the skin.

The injured areas in such cases are low and beneath the inguinal canals, and are not encountered when the transverse incision is used.

The location of inguinal hernias is such as to make it difficult to prepare them for operation, and it sometimes happens after operations for hernias that the lower end of the incision, either through infection or through an accumulation of serum at this point, does not heal well. This complication is more frequently seen when two oblique incisions have been used for the repair of double hernias, and is probably due to a greater interference to the circulation and to more extensive traumatism of the tissues in the double cases. The transverse incision heals well and entirely obviates this possibility.

This method may be applied to any case where it is desired to expose both cords or testicles. It will be found very useful in cases of double hydrocele and, as has been described by Peterson, is a useful incision in the Alexander operation for shortening the round ligaments.

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# A SIMPLE INSTRUMENT FOR TRANSFUSION\*

BERNARD FRANCIS MCGRATH

Although blood transmitted through tubes or aspirated and injected has been proved to be practically effective, yet is not that method which causes the nearest approximation to the normal vascular condition the logical one? Because of the nature of the work, desiderata in any method of transfusion are simplicity and rapidity in its execution; and an essential is sureness of flow. The

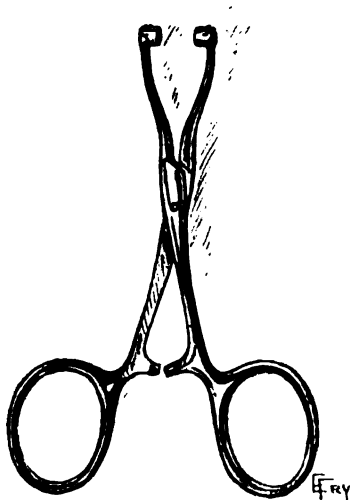


Fig. 325.—Forceps-cannula.

instrument and method of application shown in Figs. 325-328 I have found practical in experimentation. The intima of the donor is applied to the intima of the recipient in a direct line, with no foreign substance at the point of union, and only the slightest locking of the forceps is necessary to prevent leakage.

\* Reprinted from Jour. Amer. Med. Assoc., January 3, 1914, p. 40.

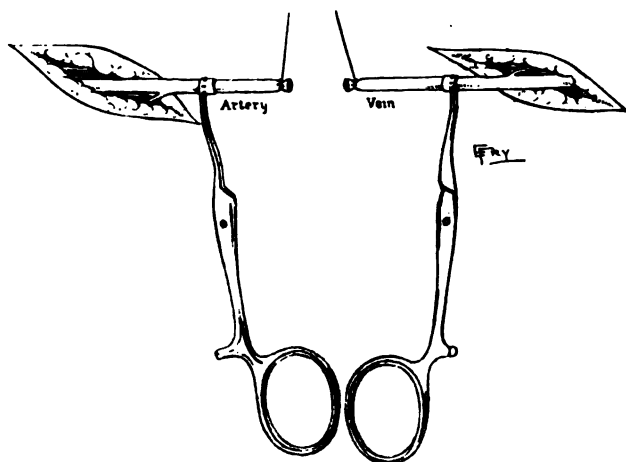


Fig. 326.—Vessels drawn through cannula by means of ends of ligatures.

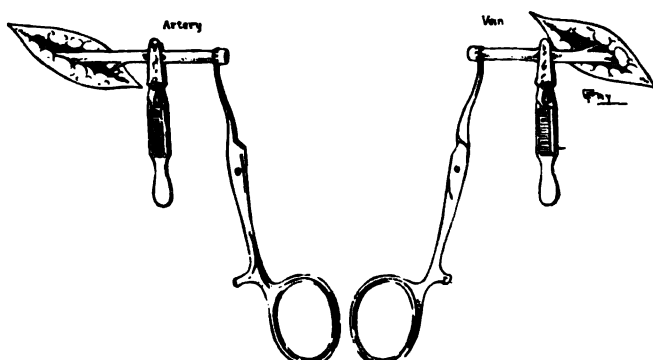


Fig. 327.—Vessels cuffed on cannula and fixed on sharp hooks.

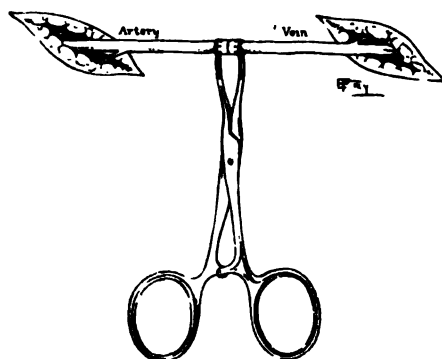


Fig. 328.—Forceps lightly clamped after allowing blood to flow from cannula.

## A SIMPLE APPARATUS FOR TRANSFUSION BY THE ASPIRATION-INJECTION METHOD\*

BERNARD FRANCIS McGRATH

In rather recent times transfusion by the method of aspiration and injection has been revived and quite frequently applied. In its favor are simplicity, sureness, and exact estimation of the amounts of blood transmitted. Different devices for the mode of transfusion have been advocated, but all are modifications of apparatus used years ago (Howe, Colin, *et al.*). Among others, the writer has found that a glass syringe with needle, or its end



Fig. 329.—Rubber bulb (about 80 c.c.) and tips for insertion into vessels of donor and recipient. No points.

drawn out to suitable size, is practicable. Anticoagulants are not essential and, probably, better avoided. The indirect method has opponents, but frequent favorable clinical reports are to be duly considered. The modification of Aneling's method, as shown in Figs. 329–332, has proved successful in the writer's experimental work. The procedure is simple and rapid in execution and positive as to results. The amount of blood transfused can be closely estimated.

\* Reprinted from Surg., Gyn. and Obst., 1914, vol. xviii.



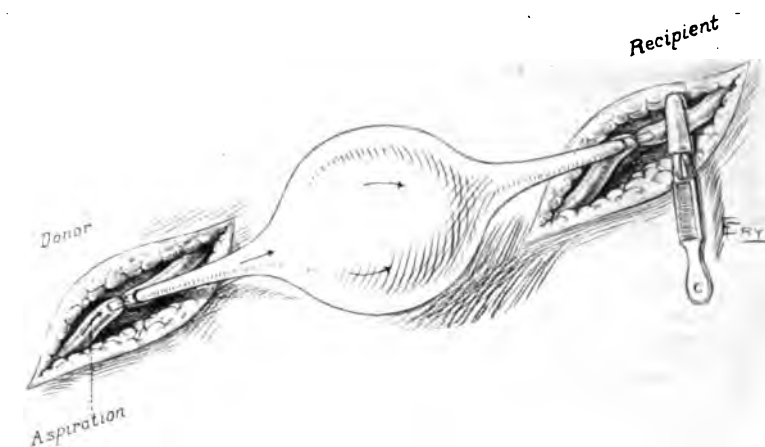


Fig. 330.—Apparatus filled with salt solution and tips fixed in vessels by ligatures. Salt solution expressed and serrefine clamp applied to recipient's vessel. Aspiration from donor's vessel until bulb is filled with blood.

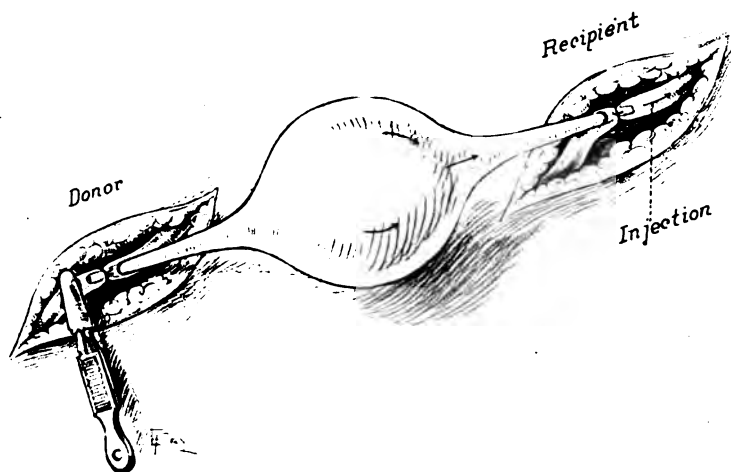


Fig. 331.—Serrefine clamp changed to donor's vessel and blood injected into recipient.



Fig. 332.—Experiment, bleeding and transfusion method: aspiration-injection, with accompanying depicted apparatus. Dogs used for experiment. Tracing of recipient. First half of record shows effect of bleeding 104.3 gm. (weight of recipient, 6041 gm.); second half of record shows effect of transfusion, the blood-pressure returning to normal in a series of elevations, each of which corresponds to an injection of blood.



## **GENERAL PAPERS**



# CARE OF SURGICAL PATIENTS\*

DONALD C. BALFOUR

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So much has been written relative to the care of surgical patients that it may appear presumptuous to attempt to offer anything worth while in the limits of a paper on this subject. I shall only synopsise the essentials of surgical treatment as they are in vogue today, which will necessitate more or less repetition of well-known and accepted principles. Some justification for this is found in the constant changes, minor in detail, it is true, which are taking place in the conduction of surgical cases. To facilitate matters I would discuss the management of these patients under four headings: (1) Care before operation; (2) care during operation; (3) postoperative treatment; (4) advice to patients.

## CARE BEFORE OPERATION

A detailed physical examination and careful recording of the findings in connection with the preoperative care are imperative. The actual preparation of the great majority of patients for operation is simple and requires of them no deviation from their usual mode of living up to the afternoon previous to the day of operation, when the patient should receive two ounces of castor oil in beer and a light evening meal. A tub-bath should be given, especial care being taken to avoid chilling, and the field of operation shaved. In the morning the lower bowel and rectum should be thoroughly evacuated by enemas, when the preparation for the operating-room is complete. This simple routine applies to the large percentage of surgical cases, while special conditions require special measures. For example:

\* Read before Sangamon Co. Med. Soc., Springfield, Ill., November 10, 1913. Reprinted from Medical Record, February 28, 1914, pp. 378-382.

(a) In all emergent cases the preliminary treatment should necessarily be abbreviated and usually omitted altogether.

(b) It is advantageous in extremely fleshy individuals in whom a radical operation for hernia is to be done to decrease the weight as much as possible by judicious dieting.

(c) There are several groups of cases in which the patient's condition makes the operative procedure of considerable risk, and in which the patient can be improved by appropriate treatment. Under this class we have:

(1) In goiters of the exophthalmic type, in which the disease is at an acute stage, the operative risk is prohibitive, and measures must be attempted to quiet the exacerbation. The preparatory treatment of these patients is extremely important and yet simple, depending as it does on absolute physical and mental rest and the use of infusion of digitalis as a cardiac corrective. Practically all drugs and local treatment have been proved to be of little definite value in these cases. The acute intoxication must subside before operative measures are attempted. Exophthalmic goiter is never a condition demanding an emergent operation, and the importance of avoiding surgical treatment during this critical period is obvious when one remembers that the operative mortality has been reduced to about 1 per cent. because of better preparation of patient and the proper selection of the type of operation. In the toxic non-hyperplastic goiters the chief lesions are of the heart and kidneys, and this group exhibits the heaviest mortality following operation. Similar preoperative care is applicable to these cases as to the typical exophthalmic group. The management of patients of both these types after their arrival in the hospital should be conducted with the greatest caution. The patient should have a room alone, and should be shown the greatest consideration, with every whim gratified if possible. We have on more than one occasion seen patients develop an acute hyperthyroidism from a definite mental irritation. A laxative should not be given these patients, because of their susceptibility to gastro-intestinal disturbance. About forty-five minutes before operation  $\frac{1}{8}$  grain morphin with  $\frac{1}{120}$  grain atropin

and  $\frac{1}{200}$  grain scopolamin should be given, the combination of which limits the secretion of mucus in the respiratory tract and more or less stupefies the majority of patients.

(2) One of the most striking examples of the value of preparatory treatment is seen in prostate cases. In these the operative results have been greatly improved by the introduction of one principle: *i. e.*, the preliminary drainage of the bladder. The opportunity this affords of clearing up the urine, maintaining the specific gravity, and of diminishing the blood-pressure has been definitely shown in the Mayo Clinic. This drainage is accomplished in some cases by a permanent catheter in the urethra; in others it is necessary to introduce a catheter through a suprapubic stab in the bladder. Crenshaw has shown that in the last 50 cases of prostatectomy in our clinic the average improvement during their preoperative care was a drop in blood-pressure from 166 to 145 mm. and the specific gravity of the urine maintained at an average of 1011.

(3) Severe anemias due to hemorrhage from uterine fibroids, bleeding ulcers of the stomach and duodenum, and hemorrhoids should be treated by large doses of iron and forced feeding. An occasional case may be suitable for transfusion shortly before operation.

(4) Patients deeply jaundiced are bad surgical risks, and if the jaundice is transitory, operation should be delayed until it has almost disappeared. The coagulation time of the blood is the most accurate indication we have as to advisability of operating, but it is also true that changes in the blood-vessels themselves are more or less responsible for their tendency to bleed easily. We have not seen any appreciable results from the use of the calcium salts, and have been disappointed in the results obtained from experiments with horse serum.

(5) The condition of emaciated patients—particularly gastric cases with obstruction at the pylorus—can often be greatly improved in the course of a few days by increasing the body fluids, by a quart of saline solution administered per rectum night and morning. All patients with suspected gastric lesions involving

retention of food should have the stomach thoroughly washed the morning of the operation.

(6) Certain cases with acute infections are benefited by careful preoperative watchfulness. Active infections in the pelvis, cholangitis, and certain stages of peritonitis are oftentimes better left undisturbed than interfered with when the patient's illness is due to a general toxemia and not to some focus of disease. These patients are still a subject of considerable controversy, but I believe the opinion is gaining ground that if they are definitely getting over the infection, it is worth while to wait for a time until some immunity is established.

(7) As regards the administration of alkaloids before operation: there is no doubt but that their use should be limited, and probably confined, to morphin and atropin. Although we are accustomed to give scopolamin to patients having exophthalmic goiter, we must admit that we believe making a routine of this practice is open to question. Morphin and atropin are given in gastric and rectal cases, in recent infections of the lung, to very fleshy individuals, to alcoholics, and occasionally to patients with heart lesions with whom local anesthesia is to be used.

#### CARE OF PATIENTS DURING OPERATION

The question of anesthesia is still a much discussed one. Ether administered through an open mask by a competent anesthetist is believed to be the most satisfactory anesthetic for the majority of cases. Ether by the intratracheal method is extremely satisfactory for certain types of cases. After the patient has been placed in the proper position on the table, and while the anesthetic is being given, the preparation of the field of operation is made. The skin is cleansed by a piece of gauze moistened by benzin to remove grease and dead epithelium, and after this has thoroughly evaporated, tincture of iodine is applied, the strength varying between 3.5 and 7 per cent. When this has dried, and the operative area is surrounded by towels, the preparation is complete.

For the welfare of the patient during the course of the operation nothing more than adherence to sound surgical principles is neces-



sary. A minimum quantity of anesthetic should be used to produce anesthesia which will be just and consistent with the surgeon's work.

Careful exploration, a not unduly prolonged operation, maintaining bodily heat, as little manipulation as possible, no more retraction of wound than is necessary to expose the parts, accurate hemostasis, and a precise toilet to complete the operation, are all factors in lessening the possibilities of postoperative complications. Rarely, if ever, are stimulants necessary or even advisable during the course of an operation. It is illogical in a patient who is markedly shocked to add further stimulation to an already overstimulated nervous system.

#### CARE OF PATIENTS AFTER OPERATION

It is true that the majority of operative cases require no special care during their convalescence, and this discussion will be confined to the treatment of special groups of cases and various complications which may arise.

Patients with toxic goiter require just as painstaking postoperative care as they received before operation. It is extremely essential that these patients obtain fluid in some way as soon as the operation is completed. As a routine, saline should be given per rectum, and in the serious cases, if this is not retained, hypodermoclysis should be used. In patients with mental restlessness or cardiac irritability ice to the head and precordium is probably of service. Drugs of any kind are of doubtful value; morphin, in some cases, is beneficial. Practically all cases should be drained following operation for goiter, the tube being removed in twenty-four hours. Acute hyperthyroidism occurring after operation for exophthalmic goiter is an extremely serious condition, and apparently no treatment is of any definite control over the intoxication, which runs a short course, terminated either by death or recovery within twelve to forty-eight hours.

The management of patients who have been operated on for lesions of the stomach and duodenum, including gastro-enterostomies, resections, and plastic operations, should follow a more or less

routine procedure. On returning from the operating-room, the patient should immediately be placed in a sitting position in bed and this maintained as much as possible for several days. This facilitates drainage of gastric fluids, and very few patients object to the upright position. Hot water in small quantities should be given after the first few hours, and if this does not cause any ill effect, it should be gradually increased, and the next day weak tea, broth, or albumin added. During the first twenty-four hours an average of two quarts of saline by bowel should be given to gastric cases. Occasionally oozing takes place into the stomach in some of these patients, and the temporary paresis causes retention of secretions and old blood. This should be carefully watched for, and if the patient is not able to vomit, gastric lavage should be carefully done with small quantities of warm water, adding soda bicarbonate if the contents are sour or acrid. The food in these cases should be gradually increased until about the time the patient leaves the hospital, when a full diet is allowed with a limitation of the heavier articles.

Another group of cases requiring special postoperative care are the prostatectomies. Here the most active attention is necessary during the first twenty-four hours to make sure the bladder is draining properly, and that the catheter or tube in the bladder is not becoming plugged with clots. As soon as drainage is removed, these patients are gotten up in order that they may not become bedridden. Undoubtedly many patients recover by reason of this forced activity who would not have otherwise done so.

Realizing the impossibility of discussing in detail the treatment of all classes of operative cases, it seems wise to limit the discussion to a consideration of the more common symptoms and complications which arise during convalescence.

*Pain.*—Pain is a variable symptom, depending on the operation, and, to a great extent, on the patient. We believe that convalescence is more rapid and more satisfactory if morphin in sufficient quantities to alleviate pain be given during the afternoon and night of the day of the operation. In very few instances will any opiate be necessary after the first twenty-four hours.

*Vomiting.*—The vomiting supposedly due to the nauseating effect of the ether is of no special moment. The vomiting which persists is of a different type, and may assume serious aspects. Sometimes an enema will relieve this condition by setting up a peristaltic action in the intestines and a passage of gas. Washing out the stomach with two or three glassfuls of warm water is sometimes all that is necessary. In other cases washing with the tube may be necessary, and in still another group, in which the condition becomes a dilatation, nothing but systematic lavage every few hours will avail. Undoubtedly many patients have been lost because this condition was not recognized, and, since the treatment is only mechanical and its efficiency so definite, little excuse can be made if a patient succumbs to such a complication. A useful adjunct in these cases of acute dilatation is to have the patient lie prone in bed with a pillow under the hips. Quite frequently this immediately relieves the condition.

*Thirst.*—Since the advent of the practice of giving fluid per rectum, thirst is not such a common complaint. In most instances as soon as the postanesthesia vomiting has ceased, the patient begins with a little hot water and if that is retained there is no further reason for limiting the supply of water.

*Gas.*—This word brings up painful recollections to many of those who have undergone abdominal operations. Drugs to stimulate peristalsis are uncertain in their effect and are not used with any frequency. Oftentimes the use of a rectal tube will relieve the patient, and enemas of various kinds should be tried, since some will be effectual where others fail. Of these remedies, the most commonly used are soap-water, plain or with turpentine, salts, and glycerin, alum, etc. If there be marked rectal irritation, milk and molasses is very satisfactory.

*Mucus.*—Mucus in the respiratory tract is sometimes very distressing, the patient who has had an abdominal operation being unable to use sufficient muscular effort to cough it up. A simple expedient is to hold the patient upright in bed, firmly supporting the abdomen by encircling his waist from behind. Braced in this

way, the patient can rid himself of the troublesome mucus with little discomfort.

*Inability to Urinate.*—Following certain operations, such as goiters, laparotomies with small incisions, etc., it is preferable to get the patient out on the side of the bed rather than to use a catheter. The use of the catheter should be limited as much as possible, since infection of the bladder may occur in the best regulated hospitals. A patient makes a bad bargain in exchanging a chronic appendicitis or a hernia for cystitis.

*Paresis.*—When of a mild degree, paresis is of no serious consequence. It is best relieved by enemas. The more prolonged types, however, are a menace, and require judgment in the treatment; the main and, at times, difficult point to be determined is whether or not the patient is overcoming the paresis. Any active interference to relieve the condition means reoperating. This same problem arises in the cases of secondary intestinal obstruction due to an adherent loop of small intestine, volvulus, etc., and the decision rests between giving the patient a chance to overcome the obstruction or to reoperate to relieve the obstruction. As a last resort, Rutherford Morison advises giving an ounce or two of castor oil. A satisfactory method of administering the oil is through the stomach-tube, after washing out the stomach. This procedure quickly settles the question, and although somewhat drastic, is justifiable. Should operative interference be considered necessary, an enterostomy is usually chosen and undoubtedly has been the means of saving many lives. The patient is usually in a precarious condition by the time such a step is decided upon; thus the shorter and simpler the procedure the better. As a rule, local anesthesia is employed. The distended loop of bowel is brought to view and, occasionally, the obstruction can be located and relieved. The enterostomy is best made by a modified Witzel method, and the bowel should be drained more or less slowly. The resulting fistula usually closes without any further attention and, should it not, a closure is readily made later.

*Complications of the Lung.*—Complications of the lung vary according to the season of the year, and quite frequently appear to be

epidemic in character. An acute condition which closely simulates pneumonia is perhaps the most common of these pulmonary complications. It usually begins on the second day following operation, with an onset suggesting pneumonia, and with the congestion of an early lobar pneumonia. This condition is maintained for two, three, or four days, without developing further than the primary stage of a true pneumonia, and then is suddenly terminated by a crisis. The essential treatment for these cases is to keep up the bodily heat of the patients, giving them all the fresh air available. Even in the coldest weather the patients may be placed in front of an open window.

*Renal Insufficiency.*—Indications of renal insufficiency should be carefully noted following operations on the urinary tract. Accurate measure must be made of the amounts of urine voided, and at any sign of failing secretion fluids should be increased and, if necessary, spartein, 3 grains, be given every three hours. In rare cases of total suppression decapsulation of the kidneys has been done with relief of the condition.

*Postoperative Hemorrhage.*—As a rule, this condition is readily recognized, but if any doubt exists, one should make absolutely certain. Deeply jaundiced cases are more treacherous in this regard, the slow coagulation-time, combined with the peculiar changes in the vessels themselves, making a secondary oozing very likely. In a few cases we have observed undoubted benefit follow transfusion, and in many cases questionable benefit from the use of horse serum. Means should always be at hand with which to perform a transfusion. Many methods of simplifying this procedure have been described recently.

*Shock.*—A true condition of postoperative shock not caused by hemorrhage, unnecessarily prolonged operations, or badly administered anesthetic, is rarely seen. When such shock does occur, saline solution subcutaneously with the aid of morphin, and camphorated oil every two or three hours, will accomplish about all that can be done.

In connection with shock the brilliant investigations of Crile have opened up a new and interesting field for study. The im-

portance of the subject and its true valuation can be determined only by time and the experiments of various observers. The benefit to be derived from blocking the peripheral nerves which are encountered in an operation would seem slight and of practical value in only a small group of cases.

*Postural Drainage.*—In acute abdominal conditions we believe that postural drainage plays a very important part in the recovery of the patient. For example: in cases of perforated appendix, with peritonitis, if the patient be kept well up in bed and lying to the extreme right side, he has a much better chance of recovery than if this principle is not followed. To render drainage efficient in these cases frequent changes of the wet dressing are advisable.

*Phlebitis.*—Phlebitis is a very distressing complication, which usually occurs about the tenth day, and involves the femoral or saphenous vein. It is not amenable to treatment other than absolute rest and local heat. The importance of rest of the affected limbs is well known because of the association with embolism.

*Embolism.*—When embolism occurs, practically no opportunity is afforded for treatment, and if there were time, we should be at a loss to know how to proceed, since no one has as yet accomplished anything in the treatment of the condition. Undoubtedly there are patients who recover permanently from pulmonary embolism, and patients may live several hours and then succumb to an attack. Embolism is one of the bugbears of surgery. The accident occurs, as a rule, just when the patient and his family are happy in the belief that all danger is past. In this connection the question arises of how long patients should be kept in bed. Our observations would not indicate that patients are in any way benefited by a prolonged stay in bed or that their being kept in bed will obviate the possibility of embolism.

#### ADVICE TO PATIENTS

The fourth point worthy of emphasis is the importance of explaining to patients recovering from a surgical operation just how to take care of themselves and what they should expect in the way of symptoms after being dismissed from the hospital. It is a mis-

take to allow patients to believe that their recovery will be complete in a month or two after an operation on the gall-bladder, stomach, or even the appendix. The postoperative treatment of these patients in the way of judicious living should continue for several months according to the type of operation. To patients who have been operated on for exophthalmic goiter should be carefully explained the possibility of a recurrence of the trouble, and all the circumstances of every case should be explained to some member of the family at the time of operation. If there is a possibility of hernia following drainage the patient should be apprised of the fact. These patients should also be told as explicitly how long to refrain from their usual work.

In conclusion I would emphasize the fact that the basis of treatment of surgical patients is simplicity. The after-care should cause little worry except in the event of complications, since the work should be completed in the operating-room. As Rutherford Morison says, "Incomplete operations are never satisfactory, and are more disastrous in their results than the most heroic, when thoughtfully planned and skilfully executed."

## A METHOD OF EXPOSING THE LOWER END OF THE URETER \*

E. S. JUDD

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The method herein described of approaching the lower part of the ureter has been employed in operating on six cases in our clinic. So far as I have been able to learn, the method has not been previously reported, and because of the many difficulties encountered in removing a small stone caught in the part of the ureter which runs through the wall of the bladder, a short description of this procedure seems not out of place.

The first patient operated on was a boy eighteen years of age with diverticulum of the bladder. The diverticulum was about three inches long and one inch in diameter, and communicated with the bladder by an opening about one-half inch in diameter in front of the meatus of the left ureter. At the cystoscopic examination a spurt of urine could be seen at the edge of the opening into the diverticulum, but a catheter was introduced into the ureter with great difficulty, evidently because of the deformity produced in the ureter by the diverticulum. The symptoms in this case were very suggestive of diverticulum, and the diagnosis was confirmed by the cystoscope.

*Operation.*—The patient was placed in a moderate Trendelenburg posture, and a median suprapubic incision made from the symphysis to the umbilicus, extending through the fascia between the recti muscles down to the peritoneum. The peritoneum was not opened, but was brushed back from the fundus of the bladder in the usual way, the bladder lifted well forward and opened after the suprapubic space had been packed off with gauze. The bladder

\* Reprinted from the *Annals of Surgery*, 1914, vol. lix.



was opened in order to explore and pack the diverticulum to facili-

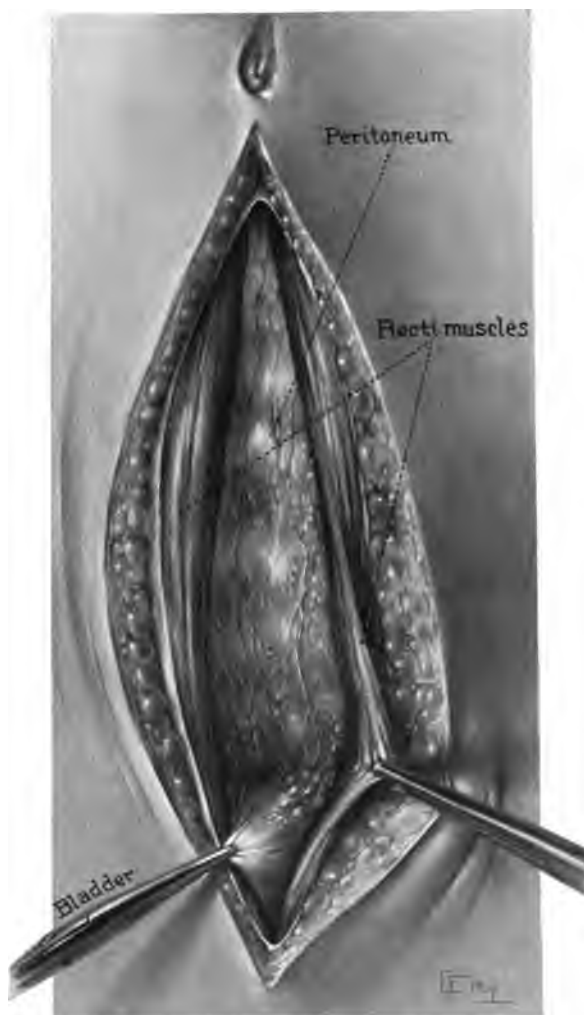


Fig. 333.—Showing regular suprapubic incision, with bladder lifted up. Peritoneum and fat have not been dissected from top of bladder.

tate in removing and also to determine, if possible, the relationship of the diverticulum and ureter so that the ureter would not be in-

jured in removing the pouch. This, however, could not be satisfactorily accomplished from within the bladder, and with the wall of the left side of the bladder held firmly by an assistant, dissection was carried down to the base of the bladder, exposing and freeing



Fig. 334.—Shows same incision with the peritoneum and fat dissected off. The bladder is held to one side by soft forceps which do not grasp the muscular wall of the bladder.

the ureter for two or three inches. The ureter was held to one side, while the diverticulum was separated from the surrounding fatty tissue and removed. The opening in the bladder was closed with the ureter in sight, so that it could not be injured or its lumen in-

terfered with. Two small rubber tissue drains were left down in the space at the side of the bladder where the diverticulum had been. These drains were removed on the third and fourth day. There had been no drainage of urine—just a little serum. The



Fig. 335.—Bladder held well to the side. Dissection through the fat shows seminal vesicle running above the ureter. Ureter dissected free for an inch or more and grasped by tacking forceps, which do not compress wall of ureter, but close it together to prevent stone slipping back if it becomes dislodged.

entire wound healed practically by primary intention, and the patient was up and around in ten days and made a complete recovery. A letter from him two months after the operation states that he is well.

In the second and third cases the operation was performed for stones in the lower ureter. In the second case a small stone was firmly lodged in the lower end of the right ureter. The Roentgenogram and the cystoscopic examinations confirmed the diagnosis. The patient, a female, aged thirty-one years, had been having repeated typical attacks of colic.

*Operation.*—The ureter was exposed as in the preceding case with the diverticulum, except that the bladder was not opened. As soon as the peritoneum had been reflected from the bladder for a little distance the right side of the bladder was retracted toward the midline and held firmly. After a very little dissection through the fat toward the base of the bladder, the stone could readily be felt. Before manipulating the stone the ureter was freed for an inch and a half or two inches above the bladder and a pair of tacking forceps were clasped across the ureter. This was done to prevent the stone from slipping up the ureter in case it became dislodged. The stone was then grasped between the fingers and removed through a small longitudinal incision in the ureter. No attempt was made to suture the opening. A rubber-tissue drain was inserted and removed on the fifth day. There was little if any leakage of urine, and the patient made a satisfactory convalescence.

In the third case, in addition to the attacks of colic due to the stone in the ureter, which was shown also by both Roentgen and cystoscopic examinations, there was also conclusive evidence of previous and recent attacks of appendicitis. In this case the patient was a male, aged twenty-seven years.

*Operation.*—As in the previous cases, the incision was made in the midline between the recti muscles. In this instance, however, it was continued through the peritoneum, and the appendix, which was subacutely inflamed, was removed. The stone in the right ureter about four inches from the bladder could readily be located by exploring from within the peritoneal cavity. After the appendix was removed the opening in the peritoneum was closed and protected by gauze pads. The ureter was exposed as in the previous cases, and a stone about  $\frac{1}{2}$  inch long and  $\frac{1}{3}$  inch in

diameter was removed. The usual rubber-tissue drains were left in the wound for several days. In this case there was drainage of some urine through the wound at first, but the wound was entirely closed within ten days.

Besides these two cases of stone in the ureter and the one of diverticulum of the bladder, the method has been used to expose the ureter in three cases of extraperitoneal resection of the bladder for cancer. In these three cases the resections were for the removal of a considerable portion of the bladder which contains one of the ureteral openings, and it was necessary to expose the ureters at this point outside of the bladder in order to transplant them satisfactorily.

With our limited experience thus far this technic seems to have some advantage over the other methods, especially for the removal of stone. The search for the ureter may be quite tedious, though if it contains a stone, as in our two cases, it can be located by using the stone as a guide. In the female the uterine artery will usually be exposed; in the male, the seminal vesicle may at first be taken for the ureter, though the difference will soon be discovered.

# NOTES FROM SOME OF THE SURGICAL CLINICS IN GERMANY, BELGIUM, AND GREAT BRITAIN—1913\*

WILLIAM J. MAYO

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When I visited the clinics of Germany, Austria, and Switzerland in 1912 several of the men whom I most desired to see were away on vacations. I therefore supplemented my trip (in May) by a short visit to the clinics of the surgeons previously missed. I then spent some time in Belgium and Great Britain.

Professor Rotter, at the Hedwig Hospital, and Professor Bumm, of the University Clinic in Berlin, are doing extraordinarily good work along special lines, that is, cancer of the rectum and cancer of the uterus, respectively. Through the courtesy and kindness of these gentlemen I was enabled to observe the work with some exactitude.

Rotter has contributed largely to our fund of knowledge concerning cancer of the rectum. His operation is a combined posterior abdominal method in one stage, with a view, on the one hand, to a thorough removal of the glands after an intraperitoneal exploration and, on the other hand, to conservation of the muscular control of the rectum. The excellent method of Hochenegg, which I have previously described,† is a single operation by the posterior route, and in the actual removal of the local disease leaves little to be desired, but no exploration of the peritoneal cavity is made for metastasis, and, so far as function is concerned, successful results would probably be somewhat less than by Rotter's technic.

Rotter operates with the patient in the reverse Trendelenburg

\* Reprinted from *Journal-Lancet*, November 15, 1913, pp. 619-626, vol. xxxiii.

† *Journal-Lancet*, August 15, 1912, pp. 423-427.

position. A posterior midline incision is made, passing to the left side of the anus with an osteoplastic flap of the coccyx turned to the right. The entire rectum, with the exception of the anal canal, is dissected free of its attachments until mobilization is so complete that it can be drawn out from behind. The patient is turned on his right side, and a long abdominal incision is made through the left rectus muscle, beginning two inches above the umbilicus and extending down to the pubic bone. The sigmoid is loosened from its lateral attachments, and, when thoroughly mobilized, the vessels are tied, the attachments cut, and the tumor with the rectum and lower sigmoid drawn out through the sacral wound. The peritoneum is carefully resutured to the sigmoid at a point where vascularization is complete, and the abdomen is closed. The patient is then turned back to the first position, and the tumor, rectum (except the anal canal), and lower sigmoid are excised. A large tube is sutured into the cut end of the sigmoid and the entire wound packed with gauze, which remains in place from eight to ten days. When granulations have formed to protect the wound, the lower end of the sigmoid is sutured to the preserved anal canal, and the osteoplastic flap is replaced. A fistula often forms, for the cure of which Rotter later turns a large flap from the buttock.

Professor Rotter is a surgeon of large experience, and has especially prepared himself for this particular operation. His aseptic technic, which is of the best, is carried out rigorously, and his results are good. Without appearing to hurry, his movements are rapid, and the operation which I witnessed was completed in a little more than an hour. I was very much impressed with his ability. In his hands the method seemed efficient and safe, but it is beyond the average operator.

As I look back over experiences in operating for cancer of the rectum in our clinic, I am tempted to say, and probably without much exaggeration, that a large percentage of the operative deaths and recurrences has been due to an attempt to conserve function, and, therefore, I can sympathize with those surgeons who believe that patients must sacrifice control in practically all cases as the price they pay for a reasonable chance of cure. Yet, when we have

removed such a rectum, and microscopic investigation has demonstrated that the entire muscular apparatus through which control comes is free from disease, we hesitate to accept the view that loss of control is a necessary part of a curative operation for rectal cancer. Surgeons are, therefore, constantly endeavoring to evolve methods and technic which will secure for these sufferers a good prospect of cure with retention of control. The majority of cancers of the rectum which occur more than three inches above the anus should be studied with a view to removal of the disease without destroying muscular control. Lesions which involve the ampulla and anal canal must necessarily be treated without regard to this question; and for this group of cases efficient methods, either in one or two stages, are at hand.

I shall refer here to the work of Mr. Lockhart Mummery, of London. I visited his clinic some three weeks after seeing Rotter, and was present while he operated on a case of cancer of the rectum. It is interesting to observe how men of different countries, often without any knowledge of the work of others, employ similar methods. In operating on these cases Mummery opens the abdomen, frees the sigmoid, resuturing the peritoneum to it, closes the abdomen, and then removes the growth with the lower sigmoid and rectum above the anal canal from behind. But instead of amputating the growth at once, he leaves it exposed in the wound, as is done in resection of the large intestine for tumor by the Mikulicz-Brun two-stage operation. On the third or fourth day the tumor, with an adequate portion of the sigmoid and rectum, is cut away and the ends sutured together. Ample provision is made for drainage. A fistula is expected to form, and closes itself, as a rule.

Mummery has a justly earned reputation for his operative work on the rectum, and his technic and results are excellent. However, I am impressed with the fact that the methods evolved by Rotter and Mummery are not for the average surgeon who must do this work, since the procedures require a high order of skill and technical knowledge, which comes from the experience only a few may gain. Yet, these operations are a step toward the operation



which will eventually be established, and which will combine the good points of these surgeons with a more simple and safe technic.

Professor Bumm, in the Universität Frauen Klinik, Berlin, has devoted much time and energy to the study of cancer of the uterus. Before visiting the clinic my interest in his work had been stimulated by the excellent review of it by Herman J. Boldt. For some years I have carefully observed the total abdominal hysterectomy for cancer as performed in various countries, and while I can agree with those surgeons who believe this method to be the best, inasmuch as it gives the highest percentage of cures, it undoubtedly is an operation which has a high operative mortality, and in from 4 to 7 per cent. of cases accidents have occurred causing injury to the bladder, rectum, and especially to the ureters. We must, therefore, welcome any improvement in technic which retains the obvious advantages of the operation and removes the disadvantages to as great an extent as possible. I believe the Bumm method of procedure to have distinct advantages. Professor Bumm has found that nitrate of silver is the best antiseptic for the vagina and cervix in these cases. His attention to the destruction of the growth by actual cautery and the preparation of the vagina for operation is thorough. In doing the abdominal operation he stands on the opposite side from the dissection which he is making. After separating both ureters and tying the uterine vessels, the vagina is caught below the cervix with a special clamp forceps; the anterior wall and then the posterior are cut across, the uterus being still attached laterally, which enables the accurate clamping and tying of these lateral structures without loss of blood. His method of protecting the bladder and ureters by stitching the peritoneum of the bladder to the anterior wall of the vagina and closing the vagina completely without drainage is a commendable feature of the operation.

For the patient afflicted with cancer of the uterus, who is in a fairly good condition, total abdominal hysterectomy offers the best chance of cure. For the poor risk, and especially the adipose individual, the vaginal method with the clamp and cautery still has a field of usefulness.

Professor Küttner, in the Breslau Clinic, is a worthy successor of Mikulicz. I do not recall having spent more profitable days in a surgical clinic than in his. Küttner is about forty-four years of age, speaks excellent English, and has the teacher's gift of imparting knowledge. Breslau is somewhat out of the way as regards location, and the clinic is not largely attended by visitors, but the opportunities for study and the work generally are so excellent that this city must again become one of the great centers of German surgery.

The University holds great interest for the surgeon since it was here the lamented Mikulicz performed his work. The clinic commands rather unusual material along the lines of bone and joint, head and spine, and gastro-intestinal lesions. I was very much pleased to observe the coöperation between the internist and the surgeon in the management of the border-line cases. In one case—an operation on the posterior spinal nerve-roots—Professor Foerster, the neurologist, gowned and gloved, took part and was intensely interested in the conditions which developed. In the larger number of operations on the brain and spinal cord the two-stage method is employed. In operations on the skull, Makkas' needle-clamp compression of the scalp is used, temporarily controlling hemorrhage, the skull being opened by a large osteoplastic flap made by an electric saw. The flap is immediately replaced and the wound temporarily closed. The operation on the brain itself followed after several days.

In operating on the spinal cord Küttner rapidly crushes the spines of the vertebræ, and with a pair of heavy scissors trims them away in a single piece. The wound is then closed, to be followed later by an operation on the nerve-roots or cord.

I observed some very interesting specimens which seemed quite at variance with the accepted views on the behavior of bone-grafts. The cases were so nearly alike that a description of one will be sufficient.

Resection of the head, neck, and greater and lesser trochanters was performed on a man with osteosarcoma of the upper end of the femur. The defect was filled from the body of a man eleven hours

dead. The patient recovered, was able to walk, and lived about two years. The entire femur sawed sagittally (postmortem) showed complete union. The muscles had reunited and, curiously enough, to their proper anatomic attachments, although not guided by sutures. Some interesting cases were shown in which bones from monkeys had been used as grafts and had not disappeared.

Küttner's work on the stomach is most interesting. He uses Graser's clamps in suturing the ends of the stomach in gastrectomy, and begins his dissection on the greater curvature, tying the gastric artery last and suturing the stomach itself from behind. In gall-bladder work he uses an incision which begins at the ensiform cartilage, and extends downward half way to the umbilicus. He then cuts two-thirds across the right rectus muscle on a line with, and about  $1\frac{1}{2}$  inches from, the margins of the ribs; the incision then passes vertically downward as far as necessary. The exposure is excellent.

At the University of Leipzig Professor Payr occupies the chair of surgery which Trendelenburg so worthily held for many years and from which he retired only a few years ago. Trendelenburg's work was markedly of great worth up to the time of his retirement. The operative removal of emboli from the pulmonary arteries was his final contribution. The "Trendelenburg position" revolutionized pelvic surgery. I had the great pleasure, when in Berlin, of driving out to Nickolasee, where Professor Trendelenburg is now living, to call on him and to convey expressions of esteem and affection from the surgeons of America.

Payr is comparatively a young man, and a prodigious worker. His clinic is most instructive. One feature of his many operating-room facilities was an idea that he had brought with him from Königsberg for cooling the room in hot weather. It is a sprinkling device that keeps the skylight and windows covered with water, and by its evaporation maintains the room at a very comfortable temperature.

Payr does a great deal of work on the stomach and in cases of gastric ulcer makes a "sleeve" resection; that is, he removes a

complete section of the stomach, greater and lesser curvature, with direct suture of the ends, shortening the stomach to that extent. His results are excellent. This is an operation which has been done extensively in our clinic for large ulcers and hour-glass stomachs with good results; but in small ulcers, where a simple excision could be readily done, we have preferred it, although, as a rule, it did not give the permanent curative results which the resection method had given in the larger ulcers. In some instances following simple excisions we were compelled to do a secondary gastro-enterostomy. Of late we have been making both the simple excision of the ulcer and the gastro-enterostomy at the primary operation unless a "sleeve" resection seemed indicated. I believe this latter method to be increasingly useful.

My purpose in visiting Erlangen was to see the work of Professor Graser, whom I had the pleasure of meeting when he was in America. I regretted that my time with him was so short. Graser is a surgeon of the first rank and in the prime of life. He has 180 hospital beds and a large amount of surgical material. He has taken a great interest in work on the stomach and has originated a method of resection for cancer which has not been excelled. He uses a special clamp of his own device which permits suturing of the closed stomach through a slot in the clamp. In doing gastrectomy, immediately after tying of the gastric artery and separating the glands of that situation, several sutures are placed, turning in the upper angle of the wall of the stomach to prevent leakage if the stomach should slip from the clamps after cutting. He makes his gastro-enterostomy, not directly opposite the mesentery, but on the inner side of the jejunum, so that two-thirds of the circumference of the small bowel lie free.

Graser's surgical activities and interests are extensive and varied. Like all the German surgeons, he is greatly interested in bone and joint work, and I examined many cases following operations for deformed and ununited fractures. In some of the deformed cases he loosens the union under an anesthetic and then applies traction for several weeks before replacement and fixation. In one case in which fracture of the femur had existed with great

deformity for some months, a nail was driven through the condyle just above the joint, thus securing direct traction on the bone. In skin grafting for circular ulcer of the leg he has shown that it is unnecessary to cover the whole ulcer at once. He has succeeded by placing strips longitudinally, and when these have become areas for growth, more strips are placed. He is using radio-active substances rather extensively and has obtained some satisfactory results in sarcoma. American surgeons traveling abroad should not miss the clinic of this warm-hearted, able Bavarian surgeon.

Professor Lexer, of Jena, has made bone and joint surgery famous in Germany by his transplantation of entire joints. He is a disciple of Bergmann, still adheres to Bergmann's technic, and has the reputation of being a surgeon who can carry out a desperate operation with skill and courage. I was present when he grafted pieces of ox-horns in place of bone. These horns are thoroughly cleansed and then slowly sterilized in front of an open fire. One case was that of a girl from whom, three weeks before, he had removed the lower six inches of the femur, including the condyles, and then closed the wound. The wound was reopened at this time, and into the cavity was placed a piece of horn about six inches long, one end of it having a door-knob enlargement for the condyles, the other having a smaller piece of horn, which connected the graft with the shaft of the girl's femur by driving it into the medulla. The wound was completely closed without drainage. Lexer told me that he had a number of such cases, and that horn was the best material unless one could secure young and growing bone from the human.

Professor Wilms, of Heidelberg, is one of the most rapid operators in Germany and he has a large amount of material. Local anesthesia is used extensively, and methods of using novocain for this purpose have been greatly extended in his clinic. I saw him perform two operations under local anesthesia for perineal removal of the enlarged prostate. Each operation was completed in about three minutes. In work on the gall-bladder Wilms operates through a straight incision, and in stones in the common duct he washes the débris from the ducts with normal saline solution.

Professor Lambotte, of Antwerp, Belgium, has a great reputation for his work in surgery of the stomach and the bones and joints, on which subjects he has written extensively. For a long time Lambotte advocated a screw-clamp arrangement somewhat like the old Parkhill clamps for the retention of fractured bones. This has been abandoned for a device much like that used by Lane. He operates by the open method for congenital dislocation of the hip on patients up to the age of twenty-five years, and with excellent results. With a large boring instrument he makes a new acetabulum, in which he places the remnant of the femoral head.

After doing gastro-enterostomy, Lambotte blocks the pylorus in a simple manner by taking a piece of twine, passing it around the stomach just above the pylorus, and tying it down sufficiently to occlude the lumen, but not so tight as to disturb circulation. He says, if tied tightly, the thread will pass into the lumen of the stomach, but with a little care it can be caused to remain as a permanent occlusion. He has been able to show, by means of radiograms, occlusion to be present after some years. I was greatly impressed with a case which was called to his attention by his assistants after the diagnosis had, apparently, been carefully worked out. A man about fifty-five years of age had sustained a Pott's fracture of the ankle-joint some months before. His foot, ankle, and leg were considerably swollen, brawny, and painful, and he had come from some distance, hoping to have this condition remedied by operation. Lambotte said promptly that the man was syphilitic, and he pointed out the characteristic appearances both in the limb and the radiograms of the bone, which his assistants had overlooked.

Mr. James Berry, of the Royal Free Hospital, London, has a large amount of material and is a most able surgeon.

This hospital is the Woman's Medical College of London, and a number of female students are in attendance.

Berry is greatly interested in goiter and has the largest material of this description in London. His work is modern in every detail and is characterized by good judgment and keen concern for the patient's welfare.

One is sometimes as much impressed with what a man does not do as with what he does do. After Berry had operated on several patients, one was brought in with extreme obstructive jaundice who had been operated on four or five times. The patient was in wretched physical condition, and after making an incision the adhesions encountered were of such a nature as almost to preclude the possibility of disentangling them. Finally, a little bile escaped from the deeper recesses of the wound. A tube was promptly placed in this spot and the operation stopped at a point where it could be taken up in the future after the jaundice had been relieved, a much better procedure than forcing the operation to a conclusion at this time.

Sir Watson Cheyne, of King's College, is well known in America, not only because of his excellent work in surgery, but also because of his literary work. Cheyne and Berghart have written one of the most popular works on surgical practice which has been published in the English language. Sir Watson is a forceful writer, a ready speaker, and a good operator. He was a pupil of Lister, whose great traditions he so worthily upholds. I was present at his clinic during a number of interesting operations. One case, that of an aged physician with carcinoma of the ascending colon, was most instructive. A resection was made, using a lateral anastomosis to bring the parts together so that the notch in the mesentery was practically closed without sutures.

I had the pleasure of seeing Mr. Thomas Walker, one of the most noted of the English surgeons in genito-urinary work. Walker is well known to Americans through his contributions to surgical literature. One of the most recent and interesting concerned the method of infection in tuberculosis of the genito-urinary tract. He shows very conclusively that the epididymis, testicles, seminal vesicles, and prostate become infected with tuberculosis along mucous paths, and that it is not hematogenous in origin, as has been widely believed. He operated on one unusual case while I was present. There were three stones in the lower ureter, which made a stone-mass the size of a pullet's egg. The transperitoneal method was employed.

One of the most interesting figures in British surgery today is W. Arbuthnot Lane, of London. In appreciation of the advances that he has made in science, Lane has recently been created a baronet.

Sir Arbuthnot, as he is now called, has been responsible for constant discussion in surgical circles during the last twenty-five years. He was the first, I believe, to tie the internal jugular vein for sinus infection in mastoid disease. In the days when the accepted treatment for cleft-palate was a dental plate, he contended for surgical methods, and now the management of such defects by the dentist is almost unknown. For years the controversy regarding the open treatment of fractures of bones was a bitter one, and Lane, alone, forced the issue which made the open method for a large variety of fractures accepted by the surgeons of the world. His theories in regard to the rôle the large intestine plays in the production of disease is being bitterly contested; and, while the question is by no means settled, each year an increasing number of men find themselves either agreeing with Lane or thinking there is more in his theories than they had believed possible.

Lane is a master technician, and a kind, considerate man, who from his quiet, modest manner would not suggest the militant spirit which has battled so forcefully for his opinions.

The ileosigmoidostomy of Lane is an operation well known to American surgeons, and is one that is now being frequently performed. It has one objection: in a certain percentage of cases the blind pouch of the large intestine, by reverse peristalsis, becomes filled with refuse material and empties itself with extreme difficulty, or possibly an impaction results. Lane now more frequently removes the large intestine. I witnessed operations on two such cases. One was so-called rheumatoid arthritis, and the other Still's disease.

Colectomy in itself is not free from objectionable features, as it necessitates the removal of the entire omentum, which occasionally results in the formation of extensive adhesions. The removal of ten inches of the ileum and all of the large intestine to the middle of the transverse colon is a comparatively easy and simple



operation and eliminates the greater part of the absorptive surface of the large intestine. From our small experience I am fain to believe that this procedure fulfils most of the indications and is free from the objections of ileosigmoidostomy and colectomy, although Lane, with his great experience, says that it is not sufficiently radical.

Three months later (August, 1913), while attending the International Medical Congress in London, I again visited Lane's clinic and observed a number of operations. Surgically considered, this work was the feature of the meeting. The operating-room at Guy's Hospital was too small to hold those who desired to see the work. One afternoon Kocher, Bier, Körte, Kümmel, Sauerbruch, Tuffier, Hartmann, Monprofit, Bastianelli, and a host of others were present. About thirty patients were shown who had been operated on months or years previously, and who apparently were cured of their former symptoms, mostly a combination of stasis and neurasthenia. Many of the statements of these patients must be taken with caution, but the history of a little girl of twelve years, fat, rosy, and active, who had doubled her weight in a year after ileosigmoidoscopy and had been completely cured of progressive "rheumatoid arthritis" of several years' standing, was most convincing. It was my privilege to go over these cases with Crile, whose experimental work in the field of internal secretions has been most extensive. Crile believes the benefit which many of Lane's patients undoubtedly derive is due to these agencies and not to the mechanical effects of the operation, *per se*.

Lane says that colectomy is unnecessary in children, short-circuiting being sufficient, and in adults, if the colon is not movable and prolapsed, ileosigmoidoscopy is efficient.

Whatever the real truth may be in regard to Lane's views on the rôle of the large intestine in the etiology of disease, they are certainly most suggestive and valuable contributions to physiologic surgery.

I may say, in passing, that Cushing's address on surgery at the International Congress was conceded to be the best of the meeting.

The work of Moynihan, of Leeds, is familiar to us all, and his

frequent visits to America have made him personally known and popular with the American profession. He has recently been knighted in merited recognition of his contributions to scientific surgery and is now known as Sir Berkeley. His contributions to surgical literature have been of the highest order, characterized by originality, a critical knowledge of literature, and clearness of diction. His views are always expressed in beautiful English. I never put down one of Moynihan's writings without a feeling of admiration for him. He maintains the same high position as a speaker; his powers of expression are graphic, and his ideas are arranged in a logical order which always makes his meaning clear.

Moynihan has a large amount of material at Leeds, and through the recent resignation of his talented colleague, Mr. Littlewood, he becomes, not only one of the great surgical figures of England, but the only one in Yorkshire. He is exceedingly generous to the younger men connected with his service at the University Hospital, advising and stimulating them in their work and giving them much material from his service. His work is characterized by careful technic and great care in details, and each part of an operation is done without haste. He is greatly interested in surgery of the stomach, duodenum, and gall-bladder, and he has made masterly contributions to the literature on these subjects. In doing gastrectomy, after freeing the tumor and stomach at the pyloric end, he performs gastro-enterostomy before cutting the diseased part of the stomach away, as it is then in condition to handle more easily than the small pouch, which remains if the operation on the stomach is completed before the gastro-enterostomy is done. He first makes an opening through the avascular arcade of the transverse mesocolon. This space is afterward utilized for the posterior gastro-enterostomy, and the gastric artery is tied from behind after the stomach has been entirely freed. Moynihan does a gastrogastrostomy instead of resection for hour-glass stomach, and he told me that in a considerable number of cases he had not failed to give relief. The method is much safer and easier than the resection which we have heretofore

practised, and it has been adopted, with excellent results, in our clinic since my return home.

Mr. Rutherford Morison, of Newcastle-on-Tyne, is the leading surgeon of Northumberland and one of the best representatives of sound, sane, and safe British surgery, of which he has been one of the leaders for more than twenty years. His contributions to surgical literature have always been of a high order. He is perhaps best known in connection with the Talma-Drummond-Morison operation for ascites from cirrhosis of the liver. Up to 1912 he had operated on 890 internal derangements of the knee-joint from fractured semilunar cartilage without a death. Newcastle is in one of the great mining sections of England, and these injuries are very frequent among the miners. I was present while he operated on two such cases. He showed me some patients on whom amputation of the penis and scrotum for cancer of the penis had been done, and the patients had remained cured for many years. He also showed cases of cancer of the vulva which had been permanently cured following extensive operation. In our experience this latter condition has seldom been followed by permanent cure after operation.

Morison is one of the men who has taken up the work of Lane, and he has had some excellent results in rheumatoid arthritis and mixed infection of tuberculous joints in children. He showed a boy, of about fourteen years of age, completely cured of tuberculosis of the hip, but, of course, with a stiff joint, a few months after ileosigmoidostomy. Photographs, etc., of the boy's former condition pictured him emaciated and with extensive sinuses in and about the hip.

Mr. Gray Turner is a student of Mr. Morison and an assistant surgeon at the University Hospital. Energetic, enthusiastic, and a keen student of surgery, Turner is a pupil to make Morison's heart glad. Turner has many little devices and improvements for the care and relief of patients following operations, which every house-surgeon ought to know and which the limitations of this article will not permit me to dwell upon. In gastro-enterostomy he puts a suture three-fourths of an inch proximal and also one

distal, uniting the jejunum to the stomach in practically the same manner that we do anterior gastro-enterostomy. In doing suprapubic prostatectomy, he has an ingenious method of drawing a pack firmly into the capsule from which the enlarged prostate has been removed, in case of much hemorrhage. One morning, after a rather tedious operation, he said: "I am not a lucky surgeon, so am compelled to take great pains." There is a whole lot in this statement.

The American student of surgery who has an opportunity to go abroad will find Newcastle-on-Tyne stimulating to a wonderful degree.

At Edinburgh I greatly enjoyed the clinics of Mr. Harold Stiles and Mr. Alexis Thomson. The work of these two surgeons is so well known to Americans that I can add comparatively little which is not already familiar.

Stiles is chief surgeon in two hospitals: the Chalmers Hospital for adults and the Royal Hospital for Sick Children. His material is enormous. In his work Stiles combines anatomic precision with great pathologic knowledge and expert handicraft. In removal of the tongue and jaw he makes a preliminary laryngotomy and packs the pharynx full of gauze. The tube is left in the larynx about three days. The work at the Children's Hospital is unique, especially in tuberculosis of bones, joints, and glands, and also in osteomyelitis.

I regret that the limits of this narrative prevent me from going into details on the many interesting features of the clinic.

Alexis Thomson is professor of surgery at the University of Edinburgh, taking this place on the retirement of John Cheine. Thomson is an excellent teacher and a sound surgeon. The treatise on surgery produced by Thomson and his colleague, Miles, while not extensive, is perhaps the best of its size in the English language. It is especially noteworthy in its balance, and while the subjects are all necessarily treated briefly, it is remarkable that the comparative space allotted to each should be so well proportioned. Thomson's activities cover a large range, and he appears to be equally at home in any department of general surgery. His re-

cent contributions to the subject of fibromatosis of the stomach and the relationships to ulcer and cancer, read before the American Surgical Association, of which society he is an honorary fellow, is one of the most masterly monographs on the subject in print.

While visiting the Royal Infirmary of Edinburgh on one occasion I was pleased to see Mr. David Wallace interrupt the course of his surgical clinic to bring in an "acute abdomen," which had just been admitted to the hospital. The delays in handling these cases, even for a few hours, are responsible for much of the mortality, a fact which Wallace was prompt to recognize and comment upon wisely.

In Liverpool I spent a day with Mr. Robert Jones, who devoted himself to the surgery of bones and joints, and here witnessed, as I have before, the most remarkable clinic of its kind in the world. Jones is surrounded by pupils from various countries, who are drawn to him by the originality of his methods. Not only is he a great diagnostician and operator, but he is also a great teacher. In speaking of tuberculosis of the spine, he said: "This disease is seldom characterized by pain or tenderness in the back, but always by muscular rigidity and in all directions. If this be absent in one direction, even if present in all others, the condition probably is not tuberculosis." In speaking of fractured semilunar cartilage in the knee he said: "Pain is felt at the exact seat of fracture, and hyperextension of the knee makes it manifest."

## LABORATORY EFFICIENCY \*

LOUIS B. WILSON

### INTRODUCTION

The idea of the technical medical laboratory is an outgrowth from two sources: First, from the older general laboratories of physics and chemistry, and, second, from the general laboratory idea which developed slowly in the clinical field of medicine. The older clinician looked upon his patient not so much as material upon which to work, as a human being with an ailment at whose nature and treatment it was his privilege to guess. Slowly there grew up, however, in the mind of the clinician, the desire to find out the story which might be told by excretions or removed tissues, and these he began to examine by chemical and physical means, adopting the methods and apparatus previously devised in the chemical and physical laboratories.

The development of the laboratory for the study of the patient has, however, been very slow, and not until the importance of teaching something of science to medical students forced itself on the attention of the medical profession were there organized any laboratories in the sense in which we now use the term. Thus teaching laboratories were the first medical laboratories to develop and long remained the standard in this and other countries. It is only within the last ten years that a medical laboratory with functions other than teaching has begun to be recognized in the medical profession. Thus we have had in the development of the pathologic laboratory particularly the somewhat anomalous condition of teaching overshadowing, if not, indeed, taking the place of, all

\* A talk before the Indianapolis Medical Society, November 25, 1913. Reprinted from the Indianapolis Med. Jour., December, 1913, pp. 512-517.

the other functions of the organization, *i. e.*, diagnosis, treatment, and research.

For I take it that the pathologic laboratory has, in common with clinical medicine and surgery, a clearly defined duty to perform in each of these four departments, namely, diagnosis, treatment, research, and teaching, and I invite your attention this evening to a consideration of efficiency in the pathologic laboratory as related to each of these four functions.

### DIAGNOSIS

When a patient is examined clinically by one man, surgically by another, and pathologically by a third, the real cause of his ailment may readily be inaccurately or incompletely formulated if either of the three depends solely upon the data which he himself has collected for the determination of the diagnosis. On the other hand, it frequently happens that neither of the three is capable of correctly interpreting the data supplied by the other two. The pathologist has properly always steered clear of finality in diagnosis except in infections and neoplasms. The reluctance of the pathologist to make a comprehensive diagnosis under other conditions is primarily due to his modest recognition of the fact that he is relatively without clinical experience. On the other hand, the clinician and the surgeon are both sometimes deficient in any similar modesty concerning their lack of pathologic experience. There can be no question but that all the data should be coördinated by the clinician, and there can equally be no question that the clinician should have sufficient knowledge of pathologic processes to interpret the data supplied by the pathologist.

Unfortunately, it is true that the average training of the clinician of today is sadly defective on the laboratory side. In his regular medical course he may have gotten a fair grounding in the general principles of pathology. After graduation he takes an internship in a general hospital where, however good his supervision in clinical matters may be, the little laboratory experience he obtains is usually without proper direction or control. After serving his internship, if, by any chance, his conscience pricks

him concerning his deficiencies in laboratory subjects, about the best he can do is to "take a course," usually in some European laboratory, where, for a fat fee, he gets a lean portion of tough facts poured into his unprepared mind. In the end he has at no time in his preparation for clinical work been compelled to investigate in the laboratory under proper guidance any problem relating to the diagnosis of any patient or to seriously attempt to solve any question relating to the cause of disease. As a result, when there come to him, concerning a patient, the data furnished, say, by a complete examination of the urine, of an examination of the blood, of an examination of the gastric contents, of an examination of the feces, of a fluoroscopic examination of the alimentary canal, and of a bit of tissue clipped from some point therein, he is wholly unable to assimilate, to coördinate, and to interpret the data obtained. Too frequently he falls back on his intuitions as to what is the matter with the patient. That thing which we call intuition in the clinician is really only the result of the working of subconsciousness on the data supplied by previous experience.

So far as the diagnostic laboratory itself is concerned, one of the greatest factors which make for its inefficiency is the presence therein of untrained men. Too frequently the surgeon and clinician, being themselves inexperienced in the difficulties of laboratory diagnosis, even of infections and neoplasms, are willing to take the dictum of some last year's graduate whose opinion on a clinical or surgical problem they would not consider for a moment, forgetting that his opinion on the results of a laboratory examination is rendered by a mind equally untrained in pathology. The untrained pathologist, when unguided, is as dangerous to the patient as he would be were he similarly unguided in his medical or surgical care of the patient. His too frequent presence without control in the diagnostic laboratory of the hospital can be accounted for by the fact that for the sake of experience he is willing to work for a small salary. His sole control of the laboratory department of a hospital is as absurd as would be the sole care of the patients clinically by the interns of such an institution. The remedy lies in the provision of more and better trained men and in their better remuneration by hospitals.



One of the most important factors of efficiency in the laboratory is the non-medical technician. This position has long been recognized in European laboratories, where the "Diener" is a highly trained man, frequently a retired petty officer from the army. The adaptation of the male "Diener" system to the American laboratory has not usually succeeded, since it is difficult to find men with sufficient education who are willing to give years to constant routine work in delicate manipulations. The solution of the problem in this country rather appears to be the high-school, or university, girl graduate; women will do routine technical work of any sort more rapidly, more accurately, and more conscientiously than will men. The labor in the laboratory is light, pleasant, and much less wearing than school-teaching. It should be better paid than school-teaching.

One word of caution concerning women as technicians. My experience has been that it is wise to avoid the "lady doctor" and the "lady nurse." Both have the idea that they have been trained for "higher things." It is very rare, indeed, that one can get either who will put the same faithful service into the work that the ex-school-teacher or high-school or college girl specially trained for the work will give to it.

The necessity for technicians is frequently overlooked, and the attempt is made to get the service done in hospitals by interns or medical students, first, because their labor is cheap and second because it is supposed to be a good thing for the embryo doctor. While both of these propositions may be true, the objections to these shifting, imperfectly trained assistants are so serious that such an arrangement should not be considered for a moment if the highest efficiency is to be expected from the laboratory. The young doctor is interested mainly in the theoretic side of things, and pays little attention to the routine technic even while engaged therein, while his term of service is usually so short that his skill is but very slightly developed by the time he leaves the service. Quite as well might the surgeon attempt to manage his sterilizing room and the routine details of his operating-room with similar help. At the same time the pathologist who attempts to get along

without technical assistants is in exactly the same position as would be the surgeon who did his own sterilizing, preparation of instruments, etc. The proportion of technicians to scientific workers in the pathologic laboratory should not be less than two to one.

The diagnostic laboratory should be in immediate apposition to the working place of the clinician and the surgeon for whom the data are intended. Some time may be wasted by the clinician visiting in the clinical diagnostic laboratory, but he is thus kept in closer touch with the results, the methods, and the ideals of the laboratory. At the same time the laboratory worker is equally benefited by close association with the clinician. Each must understand that the work of both must be closely coördinated to be of highest value to the patient and to scientific medicine. Aside from the technical coördination, good fellowship must exist between the clinical and laboratory workers, that unpleasant misunderstandings may be avoided.

All these propositions hold true for the laboratory of surgical diagnosis, and here there is also the additional factor of the necessity of immediate returns to the surgeon of data obtained from the examination of fresh tissue while the patient is still on the operating table. Ten years ago most pathologists would have smiled in a superior manner at the proposition to make a diagnosis of neoplasms or of infectious granulomas while the surgeon waited. Within the last ten years, however, we have abundantly demonstrated that not only may such diagnoses be made within a few minutes after the receipt of the tissue in the laboratory, but that they may be correctly made, and, further, that in some instances data unobtainable in fixed tissues may be found in the freshly stained tissue.

The diagnostic laboratory in close relationship to the operating-room is as important as is the sterilizing room. No hospital should be permitted to run an operating-room in which patients with tumors of doubtful malignancy are operated on unless it at the same time maintains a diagnostic laboratory and a competent pathologist.

## TREATMENT

The treatment of patients by the laboratory should be confined to those diseases in which the administration of the curative agent is a minor surgical procedure, while the immediate preparation of material to be injected is a major laboratory procedure. The very generally satisfactory administration of the Pasteur treatment for rabies by laboratory workers in Pasteur institutes all over the world for many years is the best argument for the safety and efficiency of the laboratory treatment of patients. I am inclined to think that all autogenous vaccines should be similarly administered. When we compare the great number of blunders that have been made by clinicians in the administration of such a simple and fool-proof preparation as diphtheria antitoxin, with the rare errors that have been made by laboratory workers in the administration of the exceedingly complicated treatment for rabies, there can be no question but that it is safer to trust the patient to the man who is accustomed to handling inoculation materials than it is to trust him to a man who is not so accustomed. On the other hand, I doubt whether the laboratory should be burdened by the administration of drugs of non-biologic origin, such as salvarsan. The mere fact that the Wassermann reaction is made in the laboratory is no excuse for the administration of a purely drug remedy for the disease which the laboratory man may have been called upon to help diagnose. But there is every reason for the establishment and maintenance in connection with every large hospital clinic of a laboratory for the administration of vaccine treatment for rabies, typhoid fever, acute and chronic infections, etc.

## TEACHING

The pathologic laboratory devoted to the teaching of undergraduate medical students has been the best developed, best organized, and most efficient of all types, both in this country and abroad. If I were to offer any criticism on the teaching laboratory in the high-class medical schools of this country today I should say that they fail to give sufficiently intimate knowledge of the few important things by attempting to give a general knowledge of the


many unusual and unimportant things. The course in pathology is apt to be spread out so thin over the field thus broadened that no more specific knowledge of any one topic is obtained by the medical student than he might obtain with much less effort by reading alone.

The pathologist who has a thorough working knowledge of two or three topics is far better equipped to work out for himself alone a similar useful knowledge of other topics than is the one who has only a general knowledge of a great many things. If one were revising the courses in pathology given in medical schools today, the ideal thing would be to confine the instruction in general pathology principally to inflammations and neoplasms, and in special pathology principally to perhaps half a dozen special topics.

While undergraduate teaching in the laboratories in America has been carried to a fair stage of perfection, the teaching of the graduate student has been sadly neglected. No adequate opportunity has been provided for the practising clinician or surgeon to supplement his inadequate training in pathology. The great State medical schools, at least, must come to realize their duty to provide for the physicians of the State opportunity for graduate instruction in laboratory subjects as well as in medicine and surgery. Ideally the instruction should be coördinated in the three great divisions of medicine. For some little time at Rochester we have been offering to a limited number of men an opportunity to get instruction in surgical pathology, in clinical diagnosis, and in surgical procedure by taking on, for a period of three years, properly prepared men on a Fellowship basis. These men spend one year in the laboratory, one year in clinical diagnosis, and one year in surgery. While the instruction is incidental, the opportunity for the conscientious doctor to get a fair working knowledge of the principles of each of the subjects is very good.

#### RESEARCH

The research laboratory should never be wholly dissociated from the clinical side of medicine any more than is the diagnosis laboratory, and provision for research work should be made in



the organization of every pathologic laboratory. The pathologist, even though he be relieved from the drudgery of technic by skilled technicians, will not remain long satisfied in any institution where his duties are confined to diagnosis. If he does so remain, his value to the diagnostic laboratory will rapidly deteriorate because of his lack of growth.

So far as may be, the research phase of the laboratory should be based upon the material furnished by the routine work. In this manner it is not only less esoteric but it also proceeds with less friction than when it is entirely dissociated from the routine material. Speaking generally, I should say that every scientific laboratory worker should see to it that not more than half his time at most should be occupied by routine work, the remainder to be taken up by research. By this I do not mean that the day should be equally divided into so many hours for this and so many hours for that, because the research worker who works by the hour is apt to produce very commonplace results. It is only when a man is willing to work twenty-five hours out of the twenty-four when occasion demands it that he turns out the highest quality of research work. But when such a man has spent his nights in this manner, he should not be expected to spend all of his days in teaching or in other routine work. When he has completed an investigation, or when he finds that he has gone so far that he is completely fagged out, there should be provision for his "going fishing" without the routine work suffering.

One unfortunate phase of the development of large laboratories, particularly in teaching institutions, is the enormous overgrowth of executive duties. Where these are thrown wholly on the head of the department, his time is so frequently occupied thereby that he has little opportunity for research, though he may be best equipped for this work. The delegation of these executive duties to a purchasing agent, to the heads of laboratory divisions, or even to the janitor, is to be recommended rather than that a high-class research man heading a laboratory department shall be made a hackhorse for the management of what is really the laboratory housekeeping.

## COMPLICATIONS FOLLOWING SURGICAL OPERATIONS

A REPORT OF THE COMPLICATIONS IN A SERIES OF  
6825 SURGICAL OPERATIONS PERFORMED IN  
THE MAYO CLINIC IN THE YEAR 1913

E. H. BECKMAN

The keeping of an accurate account from day to day of all the complications that occur following surgical operations is found to be an exceedingly valuable procedure. It allows one to sum up from month to month and year to year his failures and compare them with those of previous years. If this is not done, the small failures in surgical work are soon forgotten and the surgeon is inclined to feel that his results, on the whole, are better than they actually show when appearing in cold figures. It is comparable to a business firm balancing its books at the end of a period of business, and is the only true way of acquiring an accurate knowledge of the results in surgical work. If there is not a marked improvement in a diminishing number of complications, one must conclude that the cases have been exceptionally unfavorable or that his technic is not improving. As was stated in a previous report, we find that this procedure has revealed many errors in technic which it has been possible for us to overcome.

In reporting the complications that occurred in the Mayo clinic during the year 1912 it was stated that bacteriologic cultures would be made in the future from all wounds that did not heal primarily. The greater part, but not all, were subjected to bacteriologic investigation up to that time. In explanation it should

be stated that all wounds were considered as possibly infected in which there was an escape of fluid at any time during the patient's residence in the hospital. In order to secure perfect convalescence it is believed that if the technic at the time of operation is as near perfect as our present knowledge of surgical methods allows, all wounds which are not drained should be dry at the time of leaving the operating-room and should remain so until healing has occurred.

It is interesting in this connection to note that under this plan there occurred an escape of fluid from the wounds in 35 patients cultures from which developed no growth. We, therefore, consider that these wounds were not infected in the ordinary sense of the word, but that irritation or a slight accumulation of blood placed so much work upon the tissues in the neighborhood of the wound that this extra fluid could not be absorbed readily and, though sterile, was finally discharged from the wound.

In last year's report the statement was made that it appears in this clinic that most infections come from the tissues of the patients rather than from some outside source, such as suture material, dressings, or instruments. In examining the bacteriologic report for 1913 this opinion seems to be verified to a marked degree, since almost every organism identified is an organism which is commonly present in the body fluids or tissues, and that these organisms are of the type that are readily destroyed by the methods of sterilization in common use in surgical clinics. Since we know that it is impossible to kill bacteria in the tissues of the body without destroying the vitality of these structures, and that the accessories used in the operating-room, such as gloves, instruments, suture material, and dressings, can readily be sterilized, it seems more reasonable to assume that the infection comes from the patient rather than that it is introduced into the patient from some outside source. We realize, however, that this cannot always be proved, but repeated bacteriologic examinations of dressings, suture material, water, etc., used in our clinic have failed to reveal any living organisms.

The report this year includes 6825 cases, comprising the in-

patients of St. Mary's Hospital. These are the patients who had a sufficiently serious type of operation to require them to remain in the hospital during their convalescence. It does not include the out-patients having minor operations who were allowed to leave the hospital soon after their operations.

### INFECTIONS

The infections for the year 1913 were 117, or a percentage of 0.017 for the 6825 cases. The various groups of operations in which infections occurred are as follows:

TABLE I

	NUMBER OF OPERATIONS	NUMBER OF INFECTIONS
Appendectomy.....	1085	31
Nephrectomy.....	94	7
Posterior gastro-enterostomy.....	299	18
Intestinal obstruction.....	19	1
Inguinal hernia.....	308	17
Ligation superior thyroid.....	410	4
Thyroidectomy.....	1137	7
Subtotal abdominal hysterectomy.....	230	5
Freeing adhesions.....	..	1
Exploration.....	92	2
Total abdominal hysterectomy.....	79	5
Internal Alexander and appendectomy.....	117	1
Cholecystectomy.....	524	2
Bullet knee.....	1	1
Excision abdominal scar.....	1	1
Popliteal aneurysm.....	1	1
Hernia and external Alexander.....	44	1
Ventral hernia.....	76	2
Pyloroplasty and appendectomy.....	13	1
Resection stomach.....	78	2
Femoral hernia.....	29	1
Tuberculous glands neck.....	60	2
Submaxillary glands.....	47	1
Block dissection neck.....	7	2
Tubes and ovaries.....	117	1
		117



Table II shows the number of infections occurring each month, with the type of bacteria present. It is shown that more infections were present in the winter months. We believe that this is the usual rule, since the skin of the average patient is not in so good condition during these months as in the other months of the year. We have always felt that an active, healthy skin was capable of taking care of a considerable amount of infection, while one that was sluggish and irritated was in a condition to favor infection.

TABLE II.—INFECTIONS OCCURRING EACH MONTH

	No Growth	BACILLUS COLI	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS AUREUS	STAPHYLOCOCCUS CITREUS	PNEUMOCOCCUS	DIPLOCOCCUS	STREPTOCOCCUS	UNIDENTIFIED BACILLUS	BACILLUS SUBTILIS	MICROCOCCUS CATARRHALIS	NOT REPORTED	No Growth	Pure	Mixed	TOTAL
January	3	6	7	3	5	1	2	4	1	1	..	5	3	14	7	26
February	1	2	4	6	..	1	1	1	..	..	..	..	1	11	2	13
March	7	3	4	..	1	1	3	..	..	..	..	..	7	5	3	8
April	8	2	..	2	..	..	1	1	..	..	1	..	8	1	3	4
May	2	1	1	5	..	..	1	..	..	..	..	..	2	6	1	7
June	3	2	3	3	..	..	..	..	..	1	..	..	3	7	1	8
July	5	2	..	1	..	..	..	..	..	..	..	..	5	5	..	3
August and September	..	6	7	3	2	2	1	2	..	2	2	..	..	9	7	16
October	..	3	3	4	..	..	..	2	..	..	1	..	..	4	4	8
November	..	4	1	2	2	1	..	..	..	..	..	..	..	10	..	10
December	6	9	5	3	1	3	1	2	..	..	2	..	6	7	7	14
Total	35	40	35	31	12	9	10	12	1	2	6	5	35	77	35	117

Table III shows the cases that were infected with a single organism or, more properly, those that developed only a single organism in the cultures from the wounds.

TABLE III.—CASES HAVING A SINGLE ORGANISM

BACILLUS COLI	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS AUREUS	STAPHYLOCOCCUS CITREUS	PNEUMOCOCCUS	STREPTOCOCCUS	BACILLUS SUBTILIS	MICROCOCCUS CATARRHALIS
Appendectomy . 12	Right inguinal	Right inguinal	Bullet knee . . . 1	Appendectomy 1	Ventral	Appendec-	Appendec-
Nephrectomy . . 2	hernia . . . . . 1	hernia . . . . . 3	Appendectomy 1	Hernia and ex-	hernia . . . 1	tomy . . . 1	tomy . . . 1
Posterior gas-	Gastrotomy and	Left inguinal her-	Right inguinal	ternal Alex-	Right in-	Nephrec-	Thyroidec-
trotomy and	appendectomy . 1	nia . . . . . 1	hernia . . . . . 1	ander's . . . . 1	guinal	tomy and	tomy . . . 1
appendectomy 2	Left inguinal her-	Appendectomy . . 4	Gastroctomy		hernia . . . 1	appendec-	Inguinal
Intestinal ob-	nia . . . . . 1	Posterior gastro-	and appen-		Thyroidec-	tomy . . . 1	hernia . . 1
struction . . . . 1	Appendectomy . . 4	enterostomy . . . 4	dectomy . . . 1		tomy . . . . 1		
Posterior gastro-	Ligation superior	Thyroidectomy . . 2	Gastro-enteros-				
enterostomy . . 2	thyroid . . . . . 2	Posterior gastrec-	tomy . . . . . 1				
	Appendectomy	tomy and ap-	Excision abdom-				
	and right in-	pendectomy . . . 2	inal scar . . . . 1				
	guinal hernia . . 1	Total abdominal	Popliteal aneur-				
	Nephrectomy . . 2	hysterectomy . . 2	ysm . . . . . 1				
	Thyroidectomy . . 1	Exploration . . . . 1					
	Subtotal abdom-	Internal Alexan-					
	inal hysterec-	der's and ap-					
	tomy . . . . . 1	pendectomy . . . 1					
	Freeing adhesions 1	Cholecystectomy					
	Double inguinal	and appendec-					
	hernia . . . . . 1	tomy . . . . . 1					
	Exploration . . . . 1						
Total . . . . . 19	18	21	7	2	3	2	3

Table IV shows the cases in which the cultures from the wounds revealed more than one organism or a mixed culture:

TABLE IV.—CASES HAVING MORE THAN ONE ORGANISM

	BACILLUS COLI	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS CITREUS	STAPHYLOCOCCUS AUREUS	PNEUMOCOCCUS	STREPTOCOCCUS	BACILLUS SUBTILIS	UNIDENTIFIED BACILLUS	DIPLOCOCCUS	MICROCOCCUS CATARRHALIS
Left hernia . . . . .	1	..	1	..	..	..	..	..	..	..
Total abdominal hysterectomy . . . . .	..	2	1	..	1	..	..	..	..	..
Double inguinal hernia . . . . .	1	..	..	1	..	2	..	..	..	..
Ventral hernia . . . . .	..	1	..	..	..	1	..	..	..	..
Resection stomach . . . . .	..	1	..	..	..	1	..	..	..	..
Gastro-enterostomy and appendectomy . . . . .	1	1	..	..	..	1	..	1	..	..
Total abdominal hysterectomy . . . . .	1	..	..	..	1	..	..	..	1	..
Gastro-enterostomy and appendectomy . . . . .	1	..	..	..	..	..	..	..	1	..
Appendectomy . . . . .	1	1	..	..	..	..	..	..	..	..
Femoral hernia . . . . .	1	1	..	..	..	..	..	..	..	..
Appendectomy . . . . .	..	..	..	1	..	1	..	..	..	..
Tuberculous glands of neck . . . . .	..	1	..	1	1	..	..	..	..	..
Abdominal hysterectomy . . . . .	..	1	..	..	..	..	..	..	1	..
Submaxillary glands . . . . .	..	..	..	1	..	1	..	..	..	..
Appendectomy . . . . .	1	..	..	..	..	..	..	..	..	1
Abdominal hysterectomy . . . . .	..	..	..	1	..	..	..	..	1	..
Posterior gastro-enterostomy . . . . .	..	..	..	1	..	1	..	..	..	..
Tuberculous glands of neck . . . . .	..	..	..	1	..	..	..	..	1	..
Abdominal hysterectomy and appendectomy . . . . .	..	1	..	1	..	..	..	..	..	..
Hysterectomy, ovary and tube . . . . .	1	..	..	..	1	1	..	..	..	..
Block neck . . . . .	..	1	1	1	..	..	..	..	1	..
Appendectomy . . . . .	1	..	..	1	..	..	..	..	..	..
Tubes and ovary . . . . .	1	1	..	..	..	1	..	..	..	..
Nephrectomy . . . . .	1	1	..	..	..	..	..	..	..	..
Appendectomy . . . . .	1	1	..	..	..	..	..	..	..	..
Hernia . . . . .	1	..	..	1	..	..	..	..	..	..
Resection stomach . . . . .	1	..	..	..	1	..	..	..	1	1
Nephrectomy . . . . .	1	1	..	..	..	1	..	..	..	..
Gastro-enterostomy . . . . .	..	1	..	..	..	1	..	..	..	..
Appendectomy . . . . .	..	1	..	..	..	..	..	..	..	1
Anterior gastro-enterostomy . . . . .	..	..	..	..	1	..	..	..	..	1
Total abdominal hysterectomy . . . . .	1	1	..	..	..	1	..	..	..	..
Thyroidectomy . . . . .	1	1	..	..	..	1	..	..	..	..
Totals . . . . .	18	19	3	11	6	13	1	1	5	5

TABLE III.—CASES HAVING A SINGLE ORGANISM

BACILLUS COLI	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS AUREUS	STAPHYLOCOCCUS CITREUS	PNEUMOCOCCUS	STREPTOCOCCUS	BACILLUS SUBTILIS	MICROCOCCUS CATARRHALIS
Appendectomy . 12	Right inguinal	Right inguinal	Bullet knee . . . 1	Appendectomy 1	Ventral	Appendec-	Appendec-
Nephrectomy . . 2	hernia . . . . . 1	hernia . . . . . 3	Appendectomy 1	hernia . . . 1	hernia . . . 1	tony . . . 1	tony . . . 1
Posterior gas-	Gastroty and	Left inguinal her-	Right inguinal	Hernia and ex-	Right in-	Nephrec-	Thyroidec-
trotomy and	appendectomy 1	nia . . . . . 1	hernia . . . . . 1	ternal Alex-	guinal	tony and	tony . . . 1
appendectomy 2	Left inguinal her-	Appendectomy . . 4	Gastroctomy	ander's . . . . 1	hernia . . . 1	appendec-	Inguinal
Intestinal ob-	nia . . . . . 1	Posterior gastro-	and appen-		Thyroidec-	tony . . . 1	hernia . . 1
struction . . . . 1	Appendectomy . . 4	enterostomy . . . 4	dectomy . . . . 1		tony . . . . 1		
Posterior gastro-	Ligation superior	Thyroidectomy . . 2	Gastro-enteros-				
enterostomy . . 2	thyroid . . . . . 2	Posterior gastrec-	tomy . . . . . 1				
	Appendectomy	tony and ap-	Excision abdom-				
	and right in-	pendectomy . . . 2	inal scar . . . . 1				
	guinal hernia . . 1	Total abdominal	Popliteal aneur-				
	Nephrectomy . . 2	hysterectomy . . 2	ysm . . . . . 1				
	Thyroidectomy . . 1	Exploration . . . . 1					
	Subtotal abdom-	Internal Alexan-					
	inal hysterect-	der's and ap-					
	omy . . . . . 1	pendectomy . . . 1					
	Freeing adhesions 1	Cholecystectomy					
	Double inguinal	and appendec-					
	hernia . . . . . 1	tony . . . . . 1					
	Exploration . . . . 1						
Total . . . . . 19	18	21	7	2	3	2	3

Table IV shows the cases in which the cultures from the wounds revealed more than one organism or a mixed culture:

TABLE IV.—CASES HAVING MORE THAN ONE ORGANISM

	BACILLUS COLI	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS CITREUS	STAPHYLOCOCCUS AUREUS	PNEUMOCOCCUS	STREPTOCOCCUS	BACILLUS SUBTILIS	UNIDENTIFIED BACILLUS	DIPLOCOCCUS	MICROCOCCUS CATARRHALIS
Left hernia . . . . .	1		1							
Total abdominal hysterectomy . . . . .	1		1		1					
Double inguinal hernia . . . . .		2				2				
Double inguinal hernia . . . . .	1			1						
Ventral hernia . . . . .		1				1				
Resection stomach . . . . .		1				1				
Gastro-enterostomy and appendectomy . . . . .	1	1				1		1		
Total abdominal hysterectomy . . . . .	1				1					
Gastro-enterostomy and appendectomy . . . . .	1								1	
Appendectomy . . . . .	1	1								
Femoral hernia . . . . .	1	1								
Appendectomy . . . . .				1			1			
Tuberculous glands of neck . . . . .		1		1	1					
Abdominal hysterectomy . . . . .		1								1
Submaxillary glands . . . . .				1		1				
Appendectomy . . . . .	1									1
Abdominal hysterectomy . . . . .				1					1	
Posterior gastro-enterostomy . . . . .				1		1				
Tuberculous glands of neck . . . . .				1					1	
Abdominal hysterectomy and appendectomy . . . . .	1			1						
Hysterectomy, ovary and tube . . . . .	1				1	1				
Block neck . . . . .		1	1	1					1	
Appendectomy . . . . .	1			1						
Tubes and ovary . . . . .	1	1				1				
Nephrectomy . . . . .	1	1								
Appendectomy . . . . .	1	1								
Hernia . . . . .	1			1						
Resection stomach . . . . .	1				1				1	1
Nephrectomy . . . . .	1	1				1				
Gastro-enterostomy . . . . .		1				1				
Appendectomy . . . . .		1								1
Anterior gastro-enterostomy . . . . .					1					1
Total abdominal hysterectomy . . . . .	1	1				1				
Thyroidectomy . . . . .	1	1				1				
Totals . . . . .	18	19	3	11	6	13	1	1	5	5

## PULMONARY COMPLICATIONS

The total number of pulmonary complications was 87, or a percentage of 0.012 for the entire series. None of these was fatal. The deaths for the year are given in a table at the end of this paper. Ether was used exclusively in the clinic as a general anesthetic, novocain as a local anesthetic. The pulmonary complications have been classified into five groups.

GROUP I.—*Acute Postoperative Congestion of the Lungs.*—Into this group are placed those patients who disclosed acute congestion or an excess of secretion in the air-passages as soon as they were returned from the operating-room or within twenty-four hours thereafter. Many of these cases were patients that were on the verge of an acute cold, but had not revealed sufficient symptoms prior to the operation to warn the operator against proceeding. Certain others were patients that had vomited and sucked into the air-passages infectious material from the mouth and pharynx. Others were probably those that had congestion due to prolonged cooling of the air-passages from a long anesthetic. We know that an excess of secretion in the air-passages is due to irritation, so that we assume the excess in these cases must be due to some form of irritation.

TABLE V.—ACUTE POSTOPERATIVE CONGESTION OF LUNGS

Anterior gastro-enterostomy and appendectomy . . . . .	1
Excision duodenal ulcer and cholecystectomy . . . . .	1
Appendectomy . . . . .	2
Resection of stomach . . . . .	1
Inguinal hernia . . . . .	3
Appendectomy and extra-uterine pregnancy . . . . .	1
Cholecystectomy, appendectomy, and gastro-enterostomy . . . . .	1
Gastro-enterostomy and appendectomy . . . . .	1
Posterior gastro-enterostomy . . . . .	3
Splenectomy . . . . .	1
Cholecystjejunostomy . . . . .	1
Appendectomy and iliac kink . . . . .	1
Exploration of abdomen . . . . .	1
Cholecystectomy and choledochotomy . . . . .	1
Colostomy and resection of colon and urinary bladder . . . . .	1
Cholecystostomy and appendectomy . . . . .	1
Total . . . . .	21

GROUP II.—*Pleurisy*.—Patients having a pain in the chest, with or without a slight rise in temperature and a slight cough without expectoration, are classified in this group. There is often no cough or increase in temperature, but the presence of pain and a pleuritic rib on auscultation. The symptoms last from a few days to a week, rarely longer. I believe that patients operated on for pathologic conditions in the upper abdomen often have pleurisy as the result of the post-operative inflammatory reaction extending to the diaphragm and pleura.

TABLE VI.—PLEURISY

Gastro-enterostomy . . . . .	3
Supravaginal hysterectomy . . . . .	1
Cholecystectomy . . . . .	3
Resection of stomach . . . . .	1
Laparotomy for pelvic inflammation and appendectomy . . . . .	1
Appendectomy and Baldy-Webster . . . . .	1
Curetage and Baldy-Webster . . . . .	1
Appendectomy and inguinal herniotomy . . . . .	1
Nephrectomy . . . . .	1
Vaginal hysterectomy and perineorrhaphy . . . . .	1
Thyroidectomy . . . . .	1
Cholecystostomy and appendectomy . . . . .	1
Colostomy . . . . .	1
Choledochotomy . . . . .	1
Total . . . . .	18

GROUP III.—*Bronchitis*.—In this group are the patients who have an excessive secretion in the air-passages. Many of them have only a slight rise in temperature for a few days, and expectorate an excessive amount of mucus or mucopurulent material. Others have a temperature of 102° to 103° F., with increased respiration, but the symptoms subside quickly and the temperature drops to normal in from forty-eight to seventy-two hours, although the cough and expectoration may continue for several days longer. The physical examination discloses no areas of consolidation in the lungs. It is often difficult in these cases to differentiate between a congestion of the lungs, or, more properly, a congestion of the mucous membrane of the air-passages, and a true bronchitis.

TABLE VII.—ACUTE BRONCHITIS

Appendectomy.....	3
Postoperative ventral hernia.....	1
Nephrectomy, ureterectomy, cholecystostomy, and appendec- tomy.....	1
Appendectomy and posterior gastro-enterostomy.....	2
Baldy-Webster and curetage.....	1
Abdominal hysterectomy.....	1
Cholecystectomy.....	1
Exploration cancer of stomach.....	1
Choledochotomy and cholecystectomy.....	1
Excision duodenal ulcer and pyloroplasty.....	1
Pyloroplasty, Finney.....	1
Nephrectomy.....	1
Ligation right superior thyroid arteries.....	1
Closure fecal fistula and appendectomy.....	1
Closure fecal fistula.....	1
Excision duodenal ulcer and gastro-enterostomy.....	1
Gastro-enterostomy.....	2
Total.....	21

GROUP IV.—*Bronchopneumonia*.—These patients have the same symptoms as those of the preceding group, usually to a more marked degree. Inflammation here has apparently extended at certain points from the air-passages into the tissues of the lung, and the physical examination reveals areas of consolidation or congestion. Convalescence is slower than in the previous group.

TABLE VIII.—BRONCHOPNEUMONIA

Appendectomy.....	2
Resection pylorus.....	1
Gastro-enterostomy, herniotomy, and appendectomy.....	1
Posterior gastro-enterostomy.....	2
Cholecystostomy and appendectomy.....	1
Appendectomy (acute abscess).....	1
Thyroidectomy.....	1
Cholecystostomy.....	1
Enucleation of eye and postoperative ventral hernia.....	1
Pyloroplasty.....	1
Total.....	12

GROUP V.—*Lobar Pneumonia*.—In this group are those patients who have a definite consolidation of the lung with a temperature of 102° F. or more, and the classic symptoms of pneumonia. The temperature is more likely to subside by lysis than by crisis. We still believe that septic emboli cause many of these conditions.



They rarely occur earlier than the third or fourth day following operation.

TABLE IX.—LOBAR PNEUMONIA

Cholecystenterostomy.....	1
Pyloroplasty.....	2
Appendectomy.....	1
Abdominal exploration.....	1
Cholecystectomy and choledochotomy.....	1
Cholecystectomy.....	1
Thyroidectomy.....	2
Cholecystectomy and appendectomy.....	2
Gastro-enterostomy.....	2
Total abdominal hysterectomy.....	1
Anterior gastro-enterostomy.....	1
Total.....	15

### THROMBOPHLEBITIS

The total number of cases having a thrombophlebitis of the internal or external saphenous veins was 14. Table X shows the number upon the right and left sides, with the type of operation. We have not been able to determine any method of lessening this annoying complication. Most of our patients upon whom abdominal operations have been performed are out of bed by the eighth to the twelfth day, except those who have had simple appendectomies; these are allowed to get up on the sixth or seventh day following operation. There is a higher proportion of thrombophlebitis on the right side than has occurred in previous years. In our experience patients with infection are not more prone to have thrombophlebitis than the so-called clean cases.

TABLE X.—THROMBOPHLEBITIS

	RIGHT	LEFT
Nephrectomy.....	0	2
Excision duodenal ulcer, cholecystectomy, and ap- pendectomy.....	0	1
Abdominal hysterectomy.....	2	1
Cholecystostomy and anterior Hartman.....	1	0
Abdominal myomectomy.....	1	0
Vaginal hysterectomy.....	0	1
Abdominal hysterectomy.....	0	1
Cholecystostomy and appendectomy.....	1	0
Drainage large pelvic abscess.....	0	1
Gastro-enterostomy.....	1	0
Removal ovarian cyst with twisted pedicle.....	0	1
Totals.....	6	8

*Acute Dilatation of the Stomach.*—It is to be seen that during the year this complication occurred in but 3 instances. We believe this distressing complication has been avoided by frequent and early lavage. A patient who continues to vomit after the first twenty-four hours is placed upon routine lavage. The stomach is washed once or twice a day, or oftener if it seems advisable, until vomiting ceases.

The other complications listed herein are such as are apt to occur in any large surgical clinic, but are not in sufficient numbers to warrant conclusions being drawn concerning them.

#### ACUTE DILATATION OF STOMACH

Cholecystectomy and appendectomy.....	2
Cholecystectomy and choledochotomy.....	1
Total .....	3

#### EMPHYEMA CHEST

Transplantation right ureter for exstrophy bladder.....	1
---	---

#### OBSTRUCTION OF BOWELS

Resection of stomach.....	1
Resection of urinary bladder.....	1
Nephrectomy.....	1
Total.....	3

#### SURGICAL RASH

Suprapubic prostatectomy.....	1
Appendectomy and curetage.....	1
Ligation right superior thyroid artery.....	1
Cholecystostomy and anterior Hartman.....	1
Total.....	4

#### CYSTITIS

Resection of rectum.....	2
Vaginal hysterectomy.....	1
Appendectomy.....	1
Total.....	4

#### POSTOPERATIVE MISCARRIAGE

Appendectomy.....	1
-------------------	---

#### NEURITIS

Appendectomy (sciatic).....	1
Subtotal abdominal hysterectomy (arm).....	1
Total.....	2

ARTHRITIS

Appendectomy .....	1
Posterior gastro-enterostomy .....	1
Total .....	2

TONSILLITIS

Ligation superior thyroid vessels .....	2
Appendectomy .....	1
Total abdominal hysterectomy .....	1
Baldy-Webster operation .....	1
Removal lithopedion .....	1
Total .....	6

DILATATION OF HEART, ACUTE

Thyroidectomy .....	2
Ligation one superior thyroid artery .....	1
Total .....	3

DELIRIUM TREMENS

Inguinal hernia .....	1
-----------------------	---

SLIGHT BLEEDING FROM WOUND IN CASES WITH MARKED  
JAUNDICE

Cholecystectomy and choledochotomy .....	2
Secondary choledochotomy .....	1
Total .....	3

URINARY FISTULA

Total abdominal hysterectomy and removal of portion of bladder .....	1
Supravaginal hysterectomy .....	1
Total .....	2

MEASLES

Transplantation of one ureter .....	1
-------------------------------------	---

PAROTITIS

Abdominal hysterectomy .....	1
Posterior gastro-enterostomy .....	1
Ovarian cyst, dermoid with twisted pedicle .....	1
Total .....	3

SCARLATINA

Choledochotomy and cholecystectomy .....	1
--	---

## PANCREATIC FISTULA

Choledochotomy and cholecystectomy..... 1

## FISTULA FROM GASTRO-ENTEROSTOMY

Gastro-enterostomy and cholecystectomy..... 1

## ERYSIPELAS (FACIAL)

Cauterization of cancer of cervix..... 1

There were no fatalities in the cases reported above.

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